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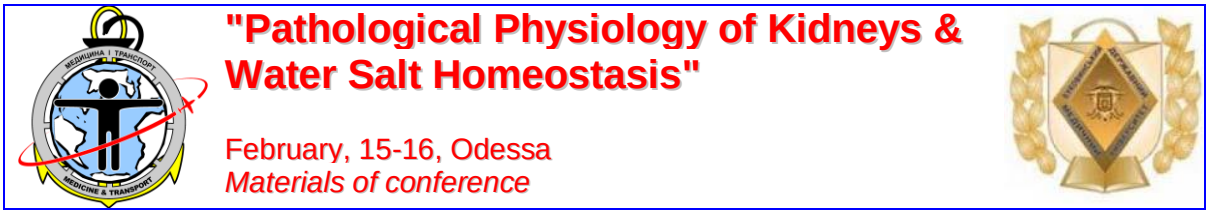

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MORPHOLOGICAL CHANGES IN KIDNEY TISSUES OF RATS WITH ACUTE ETHANOL-INDUCED INJURY AND AFTER DRUG CORRECTION

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Abstract

Kidneys perform excretory function and regulate the work of many systems of the body, therefore, the morphological changes of the functional apparatus of the kidneys must necessarily affect the functions of other organs and systems. Data on pathological processes in the kidneys caused by the action of ethanol are diverse and can be manifested as universal tissue reactions to the action of ethanol and manifestations of its toxic effects directly on the tissue of the kidney. Aim: to study the morphological changes in kidney tissues of rats with acute ethanol-induced injury and correction with quercetin and L-arginine L- glutamate. Experimental studies performed on 66 white non-linear, sexually mature male rats weighing 120-130g (average weight - 125 g). Acute alcoholic defeat was modeling by intragastric

administration of 40% ethanol in a dose of 20 ml/kg for 7 days with the help of a metal probe with oil. The revealed changes in renal tissue can be considered valuable morphological criteria that characterize the damage of the renal parenchyma in acute alcohol defeat. Using of the preparations of quercetin and L-arginine L-glutamate promotes the protection of kidney cells from the toxic effects of ethanol, which manifested itself in decreasing the severity of dystrophic changes in the endothelium of the tubules. The performed morphological study allows verifying more pronounced tread effect in the form of improving the histostructure of the kidneys under the combination of both drugs in comparison with monotherapy.

Key words: acute alcoholic defeat, rats, morphological changes, kidney, quercetin, L-arginine L-glutamate.

Introduction. According to the Ministry of Health of Ukraine, the level of drinking alcohol in the country is one of the highest in the world and is about 20 liters of absolute alcohol per person per year. Every year more than 40,000 people die of alcohol in Ukraine [6]. The effect of ethanol on the body leads to changes in many systems and organs, since it is involved in the most important processes of life. One of its leading metabolic functions is that ethanol is the source of a chemically very active and functionally important metabolite, such as acetaldehyde [5, 7]. Ethanol and acetaldehyde cause various intracellular metabolism disorders, causing damage to the membrane, imbalance of oxidation-reducing processes, energy generation impairment, nutrient deficiencies, and accumulation of toxic acetaldehyde [5, 7]. Kidneys perform excretory function and regulate the work of many systems of the body, therefore, the morphological changes of the functional apparatus of the kidneys must necessarily affect the functions of other organs and systems [3]. Data on pathological processes in the kidneys caused by the action of ethanol are diverse and can be manifested as universal tissue reactions to the action of ethanol and manifestations of its toxic effects directly on the tissue of the kidney [8]. It is known that acute kidney damage develops as a result of damage of the parenchyma, accompanied by a decrease in the intensity of tubular reabsorption, secondary damage of renal hemodynamics leads to a drop in glomerular filtration [2].

Modern preclinical studies are directed at finding the remedies that will influence the main pathogenetic links of alcoholic defeat of the kidneys, protect the tubules from damage and promote their regeneration.

Aim: to study the morphological changes in kidney tissues of rats with acute ethanol-induced injury and correction with quercetin and L-arginine L- glutamate.

Materials and methods. Experiments on animals conducted in accordance with the principles of "The Protection from abusive handling of the animals" by the Low of Ukraine (Article 230, 2006) and "the European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes" (Strasbourg, 1986) and "general ethical principles of experiments on animals" (Ukraine, 2004). The experiment conducted on base of the Department of Pathological Physiology in the Vivarium of Vinnitsya National Pirogov Memorial Medical University. Experimental studies performed on 66 white non-linear, sexually mature male rats weighing 120-130 g (average weight - 125 g). Animals were divided into five groups: 1st control - intact animals kept under standard vivarium conditions (n = 10); 2nd (n = 20) - animals with acute alcoholic defeat, conducted on the basis of the experimental model of acute alcoholic hepatitis (AAH) [4] - by intragastric administration of 40% ethanol in a dose of 20 ml / kg for 7 days with the help of a metal probe with oil; 3rd group - animals with AAH (n = 12), which were intraperitoneally injected with the water-soluble form of quercetin - "Korvitin" (JSC "Borshchagovsky Chemical and Pharmaceutical Plant", Kyiv) at a rate of 100 mg / kg; 4th animals with AAH (n = 12), which were injected intraperitoneally with L-arginine L-glulamate (Glutargin, LLC "Pharmaceutical company "Zdorovya", Kharkiv) at a rate of 40 mg / kg; 5th - Animals with AAH (n = 12) who received intraperitoneally quercetin 100 mg / kg and L-arginine L-glulamate at a rate of 40 mg/kg. After removing the animals from the experiment under the thiopental anesthesia (at a rate of 25 mg / kg), the kidney tissues were collected for histological examination. Kidney specimens were fixed by immersion in 10% neutral buffered formaldehyde solution for 48 h and then dehydrated in a graded series of ethanol solutions, and embedded in paraffin at a temperature of 58ºC. Histological tissue sections (5 mm thick) were received and stained with hematoxylin and eosin to assess the morphology.

Analysis of the research. At histological examination of the structural components of the kidneys of rats receiving ethanol without the correction, signs of parenchymal degeneration of the convoluted tubules were revealed (Figure 1). Blood flow is somewhat more pronounced in the brain layer. Blood filling of glomerular capillaries is uneven in the course of sections. In the lumen of the vessels, we observed a plasma detachment from the formed elements. In most fields of view, glomeruli are not enlarged, but sometimes there are isolated hypertrophied glomeruli. In the lumen of capsules of individual glomeruli, pink homogeneous masses appear. The epithelium of the convoluted tubules is swollen, some lumens of the tubules are considerably narrowed; the cytoplasm of most cells is granular. The nuclei are pale colored, their chromatine is sparse, there is swelling of the stroma, which is

more pronounced in the medullar layer. Shallow focal hemorrhages in the stroma of the medullar layer were detected.

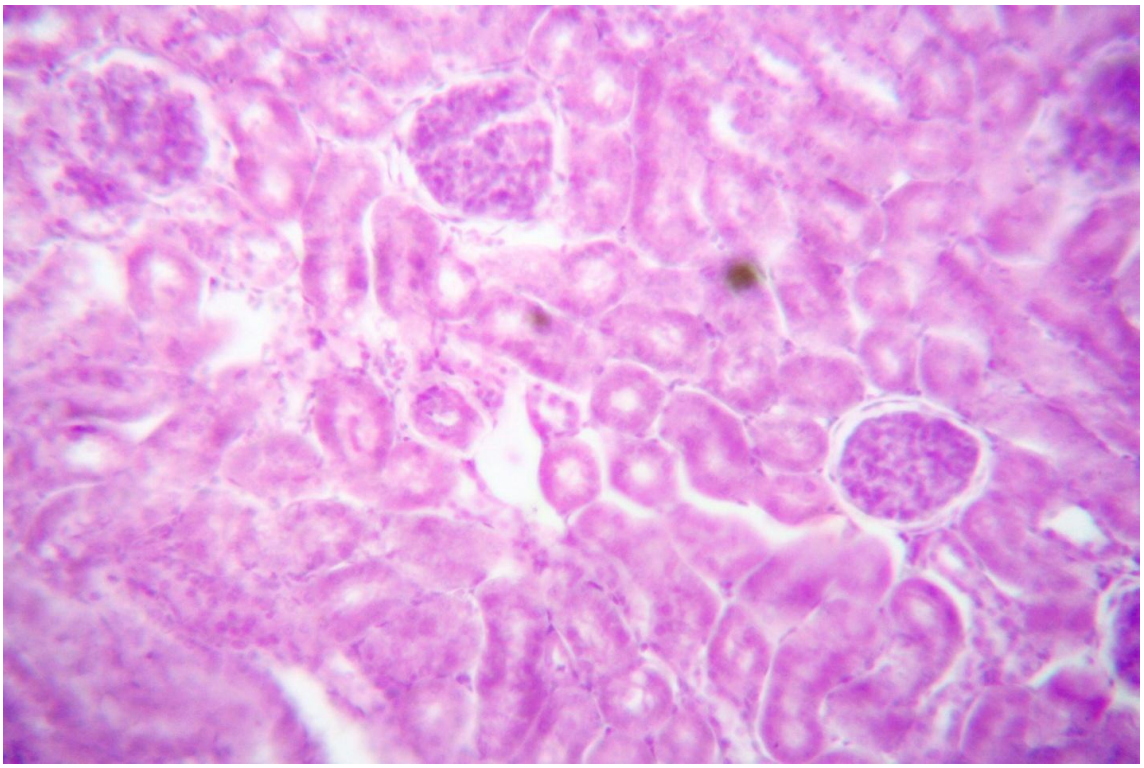

Fig. 1. Histopathological changes in the kidneys of rats with acute ethanol-induced injury. Hematoxylin and eosin ×100.

When applying quercetin for correction the toxic effects of ethanol in the renal tissue, the following changes are detected. Uneven blood flow to the vessels along the sections. Often in the lumen of the vessels there is a plasma separation. The glomeruli is of almost the same size. Lumens of capsules are well-pronounced, sometimes containing pink granular masses. Signs of parenchymatous dystrophy of the convoluted tubules are less pronounced than in the previous group. The epithelium of the tubules is swollen, cells of the cytoplasm are granular, somewhere homogenized, cloudy. The nuclei in most fields of view are normochromic, only in separate fields chromatin nuclei are pale (Figure 2).

In animals, which were injected with L-arginine L-glutamate for the correction of acute alcohol defeat, the following changes were observed. There is uneven blood filling of the vessels in both layers, however, it is less distinct in animals of 2nd group. The glomeruli are not enlarged, the lumens of the capsules are expressed unevenly along the sections. The epithelium of the convoluted tubules is swollen, the tubules' lumens are slightly narrowed (Figure 3).

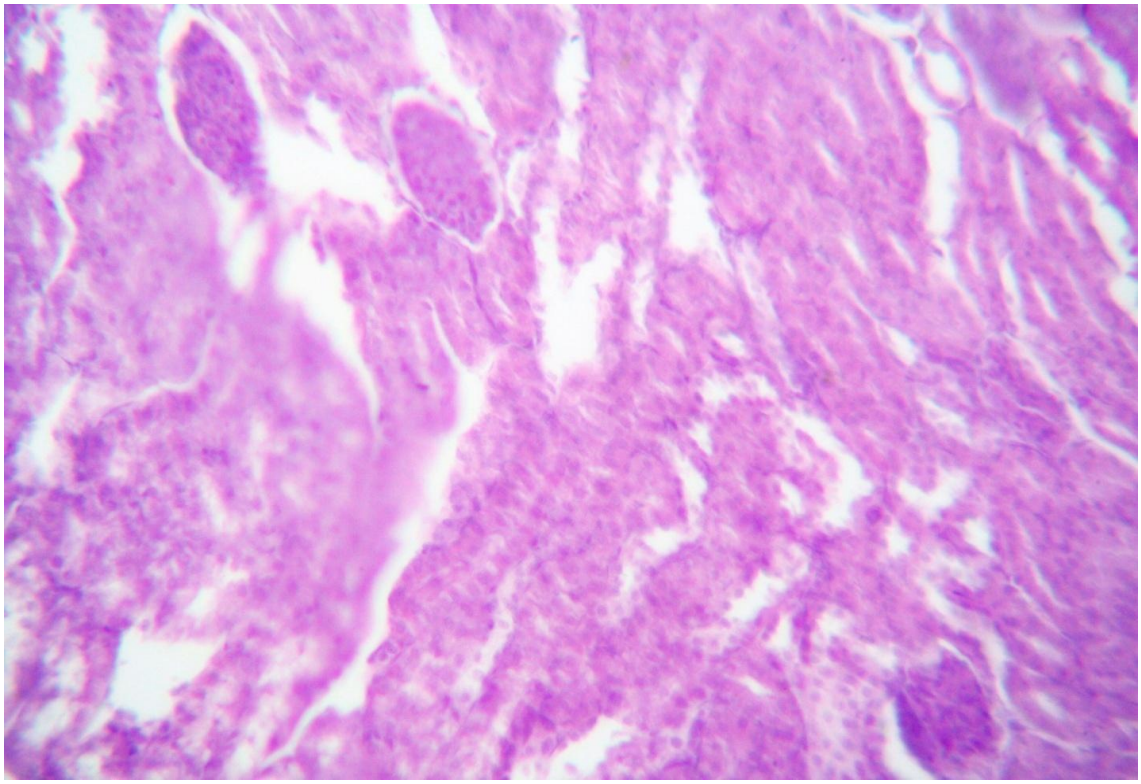

Fig. 2. Histopathological changes in the kidneys of rats with acute ethanol-induced injury and correction with quercetin. Hematoxylin and eosin ×100.

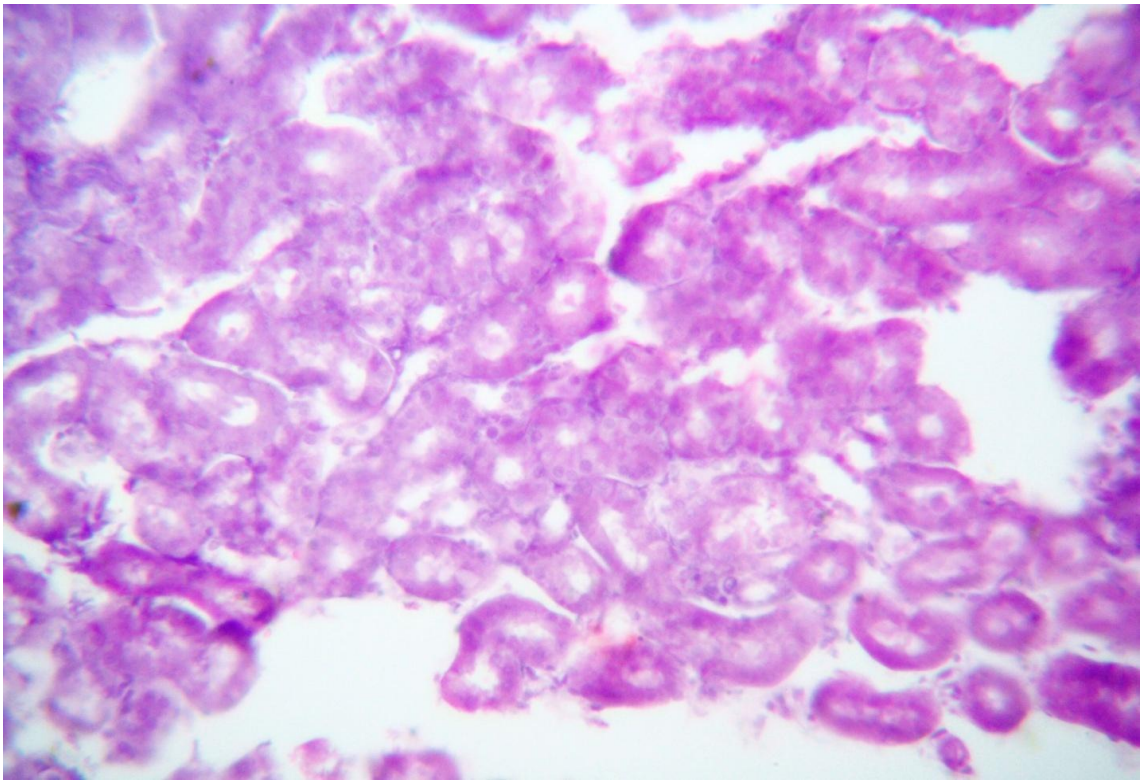

Fig. 3. Histopathological changes in the kidneys of rats with acute ethanol-induced injury and correction with L-arginine L- glutamate. Hematoxylin and eosin ×100

Significant changes in the structure of the kidneys are observed in animals of group 5, which correction of toxic effects of ethanol was carried out simultaneously with the use of quercetin and L-arginine L-glutamate. As in previous animal groups, blood vessels are unevenly filled in both layers, but visually less distinct than untreated animals. In the cortical layer, the glomeruli are almost of the same size. Glomerular capsules are well expressed, optically free, only somewhere contain pink granular masses. Lumens of tubules are free. The epithelium of the convoluted tubules is swollen. In the majority of epithelial cells there is a decrease in the manifestations of dystrophy, only in the single cells cytoplasm contains granularity (Figure 4).

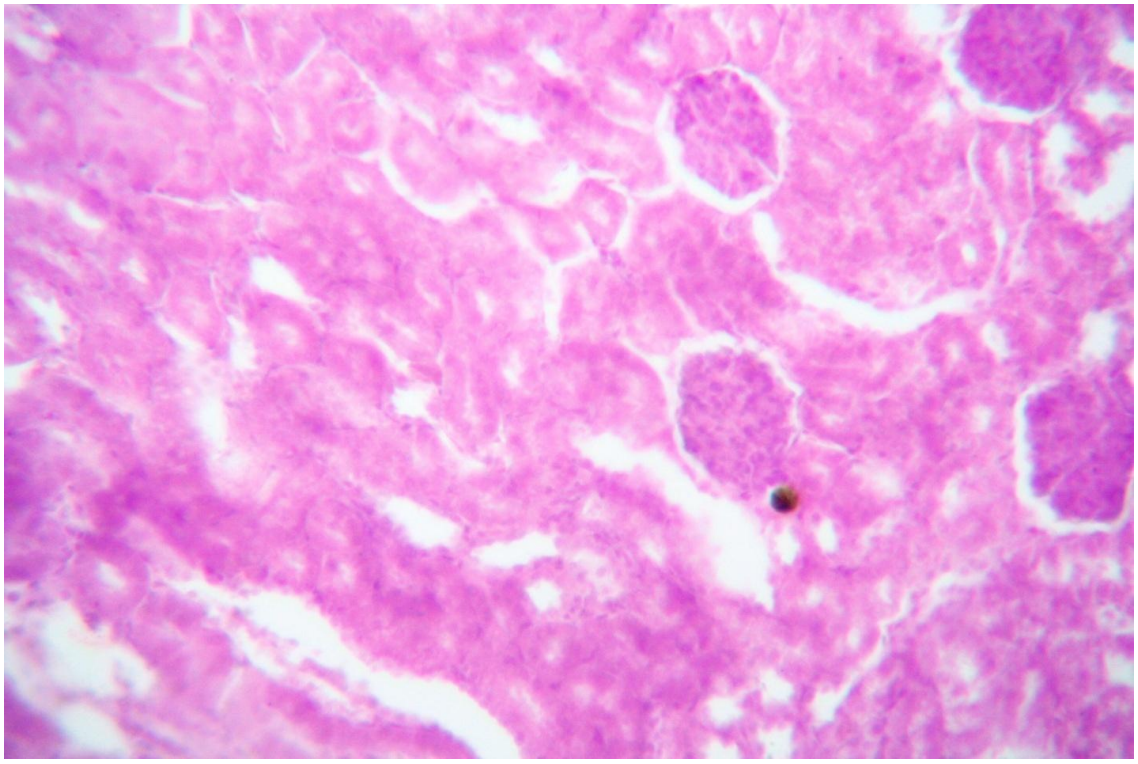

Fig. 4. Histopathological changes in the kidneys of rats with acute ethanol-induced injury and correction with quercetin and L-arginine L- glutamate. Hematoxylin and eosin ×100

We compared the revealed changes in the structural components of the kidney of rats with acute alcoholic defeat with the results of histological examination of kidney of rats under medicamentous impartment [1]. The similar structural changes such as diffuse venous-capillary hypertrophy, mainly medullar layer, parenchymal dystrophy of the convoluted tubules, hypochromic nuclei, as well as edema of the epithelium of the convoluted tubules,

the narrowing of their lumen revealed in both alcoholic and medicamentous toxic lesions of the kidneys.

Conclusions

1. Thus, the revealed changes in renal tissue can be considered, valuable morphological criteria that characterize the damage of the renal parenchyma in acute alcohol defeat.

2. Using of the preparations of quercetin and L-arginine L-glutamate promotes the protection of kidney cells from the toxic effects of ethanol, which manifested itself in decreasing the severity of dystrophic changes in the endothelium of the tubules.

3. The performed morphological study allows verifying the more pronounced tread effect in the form of improving the histostructure of the kidneys under the combination of both drugs in comparison with monotherapy.

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