UDC 616:61-092.9:576.31:616.831-005.1

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MORPHOLOGICAL CHANGES IN THE KIDNEYS OF RATS WITH EXPERIMENTAL HEMORAGHICAL STROKE (ITRACEREBRAL HEMORRHAGE).

Key words: hemorrhagic stroke, experiment, structural changes of the kidney.

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Hemorrhagic stroke is not limited with ischemic damage of the brain tissue and affects the function of other organs. A stroke is considered as a complication in the context of renal failure, but renal dysfunction following a stroke has not been sufficiently investigated. Only in some studies it has been shown that the state of renal function in patients with hemorrhagic stroke affects the quality of the life, in particular, is a mortality factor in the first 10 years [Tsagalis, 2009]. The high frequency of hypertonic nephropathy of patients with hemorrhagic stroke was detected (almost 70%) [Shemetova, 2012]. The number of these patients varies significantly between studies. According to various data, the occurrence of renal dysfunction is noted from 2% to 53% of patients [Covic, 2008; Kamouchi, 2013]. The presence of moderate and severe renal insufficiency of patients with hemorrhagic stroke is associated with the volume of hemorrhage and a weak recovery [Molshatzk, 2011]. The authors note that the presence of moderate renal dysfunction is an independent factor in a new episode of cerebral circulation disorder.

The pathophysiological mechanisms that mediate the increased risk of hemorrhagic stroke in chronic renal failure are not definitively identified, but may be associated with such factors as accelerated vascular calcification and atherosclerosis, hypercreatininuria, changes in rheological blood parameters [Power, 2013]. In this case, the pharmacotherapy of hemorrhagic stroke can affect the condition of the kidneys. Yes, hypertonic solutions and mannitol can cause kidney dysfunction [Khatri, 2014]. Taking into account these data, the purpose of the work was to investigate the morphological changes of the kidneys in a hemorrhagic stroke.

Materials and methods

The experiments were performed on Wistar rats with a weight 210-230 g. The hemorrhagic stroke was modeled by introducing an autoblood injection into an internal capsule of the animals (capsule interna, L = 3.5-4.0; H = 6.0; AP = -2) (n = 7). For this purpose, in the temporal bone of the rats, a hole with a diameter of 1 mm was carried out. Blood was obtained from the tail artery and injected into the brain after a previous stereotactic destruction in order to form a local hematoma. Manipulations were performed on the right hemisphere. The volume of administration of autoblood was 0.1-0.2 ml. On the 3rd and 21st day after the surgery, the rats were withdrawn from the experiment.

The control group consisted of intact rats (n = 3) and rats after trepanation of the temporal bone but without introduction of an autoblood (n = 3); The experimental group consisted of 6 animals. All manipulations with animals were performed under anesthesia (sodium thiopental, 60 mg / kg, intraperitoneally).

The statistical processing of the received data was carried out by using standard methods of processing of the results in the Excel editor. The differences between the groups were assessed using Student's t-criterion, and results with a significance level of more than 95% were considered as reliable ($p < 0,05$).

Research results

The changes in the a behavior and signs of neurological deficiency of the rats with hemorrhagic stroke were recorded on the 1-4 days of observation. The death was noted only in one case. In the following 5-21 days, signs of neurological disorders were reduced. The model of hemorrhagic stroke is characterized by the simplicity of reproduction, the formation of neurological disorders and low mortality. The rats were extracted from the experiment on 3rd (n = 3) and 21st (n = 3) day of observation. The histological method confirmed the localization of hemorrhage in the right inner capsule of the brain and neurodegenerative changes in the cerebral cortex of the experimental rats (Fig. 1).

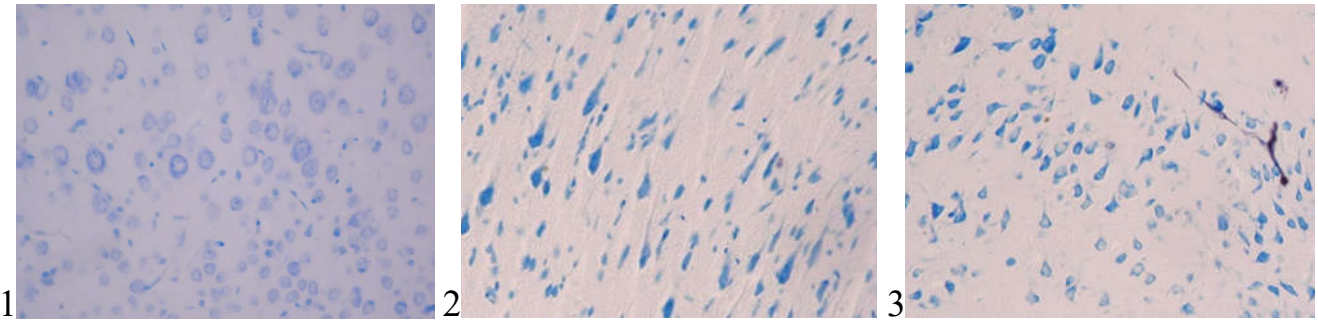
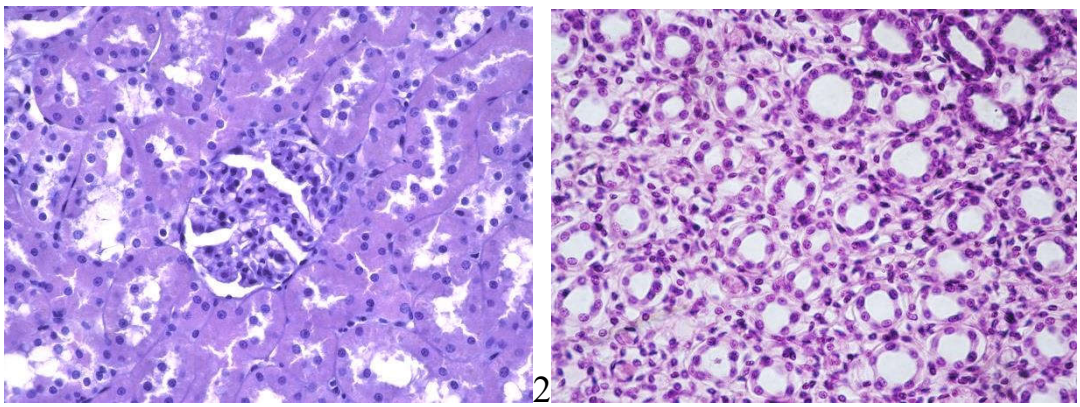


Fig. 1. Sensomotor region of the cerebral cortex of the control and experimental groups of the rats.

Note: 1 - intact animals; 2 - stroke rat on 3rd day; 3 - rat with a stroke on 21st day. Crezyl violet stain, × 200.

Figure 2 shows the microslide of kidney of a rat with hemorrhagic stroke. The structural changes of the right and left kidneys were separately compared in order to detect the difference in the localization of violations. In all investigated samples of experimental rats, cortex and medulla were recorded. In the cortex (on a 3rd day of observation) nephrons, vivid nephron tubules were observed. Interstitial edema was not detected, but in some tubules there were an increase in lumen and dystrophic changes in individual epithelial cells. In the medulla, the diameter of the thick tubules of the nephrons in the left kidney decreased, the right kidney was without statistically significant difference (Table 1). The reductions in quantitative values were associated with the loss of a part of the thick tubules, which was associated with their edema, dystrophic changes in the epithelium of the tubules, and destruction, i.e. tubulone-necrosis and tubulorexis. A quantitative estimate was made only on structurally preserved tubules of smaller diameter.

In the remote period (21st day of the observation), cortex and medulla were also clearly differentiated. In the cortex, there were nephrons, ventricular tubules, also the reduction of tubular and internal edema was marked. According to the results of the histological study of the medulla, the tendency to reduction of cytological violations of the epithelium of the left renal tubules has also been noted, while in the right kidney the structurally damaged tubules of the nephrons and the tubular buds of the renal papilla continued to be recorded. On the basis of these data, it can be assumed that the rats` kidney were damaged at the 3rd day of the stroke and there were a partial recovery on 21st day.



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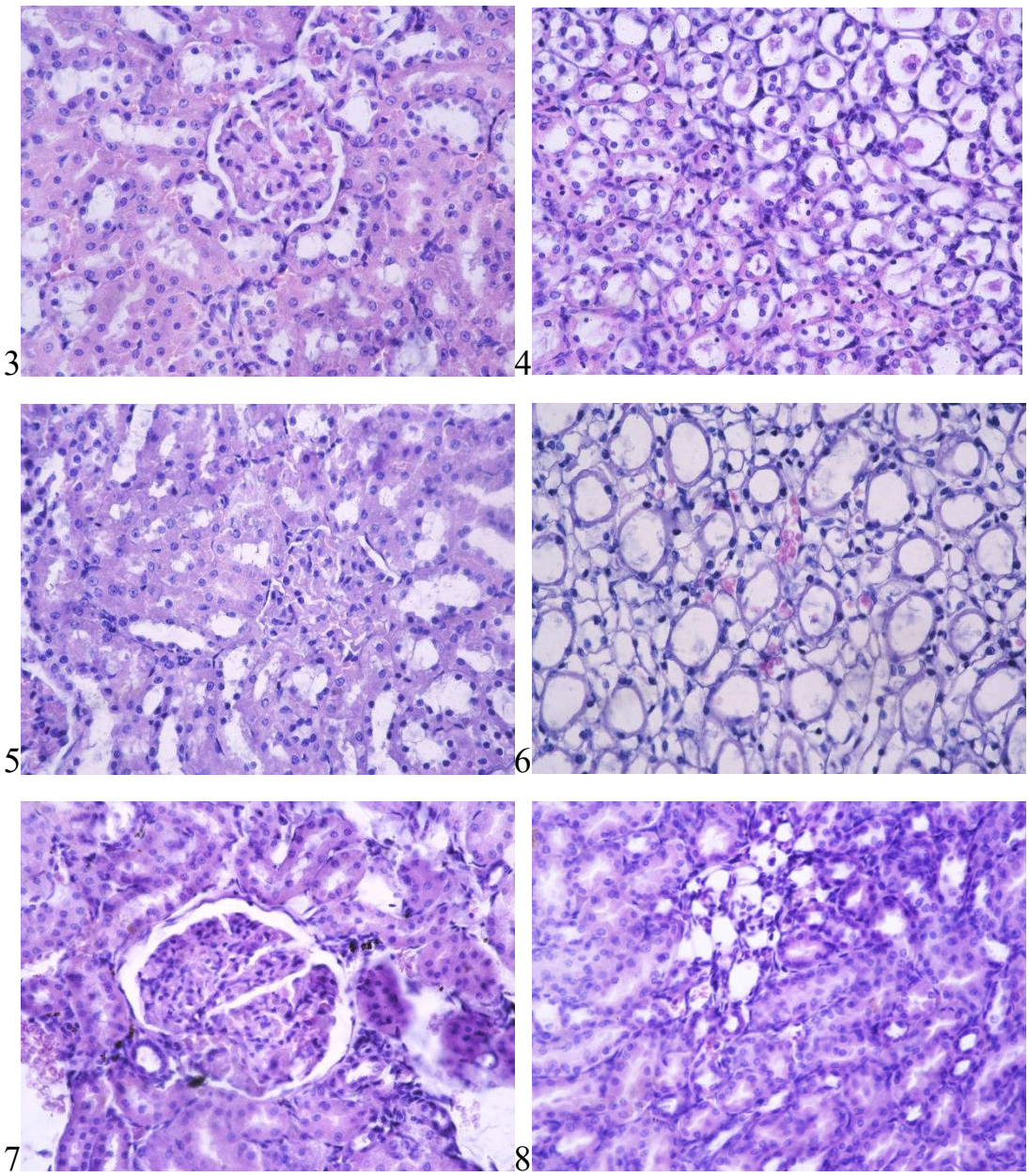

Fig. 2. The results of the histological examination of kidney of rat with hemorrhagic stroke. Structural changes of the thick tubules of the nephrons of the medulla of the kidney and of the collecting tubules of the kidney. Note: 1,2 - intact rats; 3.4 - left kidney of rats with stroke on 3rd day; 5.6 - right kidney of rats with a stroke on 3rd day; 7.8 - left kidney of rats with stroke on 21st day; 9,10 - right kidney of rats with a stroke on 21st day; 1,3,5,7,9 – kidney cortex; 2,4,6,8,10 - kidney medulla. Hematoxylin-eosin stain, × 400.

Table 1. The results of the morphometric evaluation of structural changes in kidneys of rats with stroke

№	The group	Morphometric parameters

		Diameter of proximal tubules of the cortex, mkm	Diameter of thick tubules of the medulla, mkm
1	Control	68,3±2,17	50,1±1,70
2	Left kidney, 3rd day	56,9±1,58*	45,3±1,10*
3	Right kidney, 3rd day	52,9±1,67*	49,0±1,60
4	Left kidney, 21st day	46,9±1,22*#	36,5±0,77*#
5	Right kidney, 21st day	51,1±1,43*	40,5±0,85*#

Note: * - Reliable to control ($p < 0,05$); # - Relatively up to 3 days ($p < 0,05$)

Discussion

The analysis of literary sources indicates a low level of study of morphological changes in the kidneys against the background of impaired cerebral circulation. Systemic kidney function analysis is described only in some clinical trials [Hamed 2015], and structural violations are described only occasionally in individual experimental work. The authors note the changes in microcirculation in the renal tissue of rats with spontaneous hypertension and hemorrhagic stroke, mainly in the small and medium interglomerulal arteries of the cortex [Rocha 1999]. A significant variability of necrotic changes is possible. Thus, in the kidneys without significant violations of the necrosis, it was rarely observed (<2%), while parenchyma necrosis was combined with the appearance of fibrin deposits in vessels in 20-45% of the samples under study [Tanaka 2001]. This is supposed to be an ischemic lesion of capillary glomeruli, which is associated with interstitial impregnation with erythrocytes, occlusion of pleural arterioles. Such changes are formed in the period of 14 days, but the data that would describe the subsequent changes in the remote term is not described. The described histological studies provide a new data on the development of structural changes in the kidney medullar of rats with hemorrhagic stroke, which can be associated with disturbed exchange of electrolytes at the level of the distal segment of the nephrons. Nevertheless, we agree with the authors on the progressive nature of the development of structural changes in the nephrons.

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