

Gozhenko A. I., Bibikova V. N. Morphological changes in the kidneys of rats with experimental hemorrhagic stroke (intracerebral hemorrhage). *Journal of Education, Health and Sport*. 2018;8(1):254-262. eISSN 2391-8306. DOI <http://dx.doi.org/10.5281/zenodo.1202357>
<http://ojs.ukw.edu.pl/index.php/johs/article/view/5368>

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part B item 1223 (26.01.2017).
1223 Journal of Education, Health and Sport eISSN 2391-8306 7

© The Authors 2018;

This article is published with open access at Licensee Open Journal Systems of Kazimierz Wielki University in Bydgoszcz, Poland



Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non Commercial License

(<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

This is an open access article licensed under the terms of the Creative Commons Attribution Non Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 23.01.2018. Revised: 26.01.2018. Accepted: 31.01.2018.

	"Pathological Physiology of Kidneys & Water Salt Homeostasis" February, 15-16, Odessa <i>Materials of conference</i>	
---	---	---

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

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

A. I. Gozhenko¹, V. N. Bibikova²

¹Ukrainian Research Institute for Medicine of Transport

²State Establishment "Dnipropetrovsk Medical Academy of Health Ministry of Ukraine",

department of pathological physiology (acting head of the department –
prof., D.Sci. Koldunov Victor Vladimirovich)

Abstract

The article presents the results of the study of morphological changes in the kidneys in Wistar rats during the stroke. Hemorrhagic stroke modeling was performed by injecting 0.1-0.2 ml of autoblood through an opening in the temporal bone into the region of the inner capsule of the right hemisphere. To form a hematoma, a stereotaxic destruction was performed. The experimental group consisted of 6 animals, the control group was represented by intact rats (n=3) and rats after trepanation of the temporal bone but without the

introduction of autoblood (n=3). The animals were removed from the experiment on days 3 and 21. In the course of the study, the structural changes in the right and left kidneys were compared to determine the difference in the location of the disorders. According to the results of the histological examination of the medulla, the tendency to reduction of cytological disorders of the epithelium of the tubules of the left kidney was revealed, while in the right kidney the structural disturbances of the tubules of the nephrons and the collecting ducts of the papilla of the kidney were recorded. Based on these data, it is possible to assume renal involvement in rats on day 3 after a stroke and a frequency recovery on day 21. The described histological studies give a new data on the development of structural changes in renal medulla in rats with hemorrhagic stroke, which can be associated with a violation of electrolyte exchanges at the level of the distal nephron segment.

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

**МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ ПОЧЕК У КРЫС С
ЭКСПЕРИМЕНТАЛЬНЫМ ГЕМОМРАГИЧНЫМ ИНСУЛЬТОМ
(ВНУТРИМОЗГОВОМ КРОВОИЗЛИЯНИИ)**

А. И. Гоженко¹, В. Н. Бибилова²

Украинский НИИ медицины транспорта

²ДУ «ДМА МЗ Украины», кафедра патологической физиологии

(и.о. заведующего кафедрой – проф., д.мед.н. Колдунов Виктор Владимирович)

Резюме

В статье представлены результаты исследования морфологических изменений почек у крыс линии Вистар при геморрагической инсульте. Моделирование инсульта проводилось введением 0,1-0,2 мл аутокрови через отверстие в височной кости в область внутренней капсулы правой гемисферы. С целью формирования гематомы была произведена стереотаксическая деструкция. Экспериментальная группа состояла из 6 животных, контрольная группа представлена интактными крысами (n=3) и крысами после трепанации височной кости но без введения аутокрови (n=3). Животных выводили из эксперимента на 3 и 21 дни. В ходе исследования сравнивали структурные изменения правой и левой почек с целью выявления разницы локализации нарушений. По результатам гистологического исследования мозгового вещества выявлена

тенденция к редукции цитологических нарушений эпителия канальцев левой почки, при этом в правой почке регистрировались структурные нарушения канальцев нефронов и собирательных канальцев сосочка почки. На основании этих данных можно предположить поражение почек у крыс на 3 сутки после геморрагического инсульта и частичное восстановление на 21 сутки. Описанные гистологические исследования дают новые данные о развитии структурных изменений в мозговом веществе почек у крыс с геморрагическим инсультом, что можно связать с нарушением обмена электролитов на уровне дистального сегмента нефронов.

Ключевые слова: геморрагический инсульт, эксперимент, структурные изменения почек.

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 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).

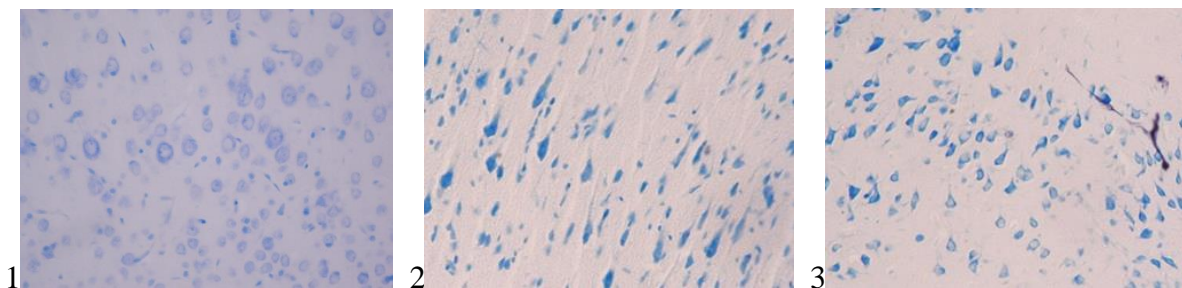
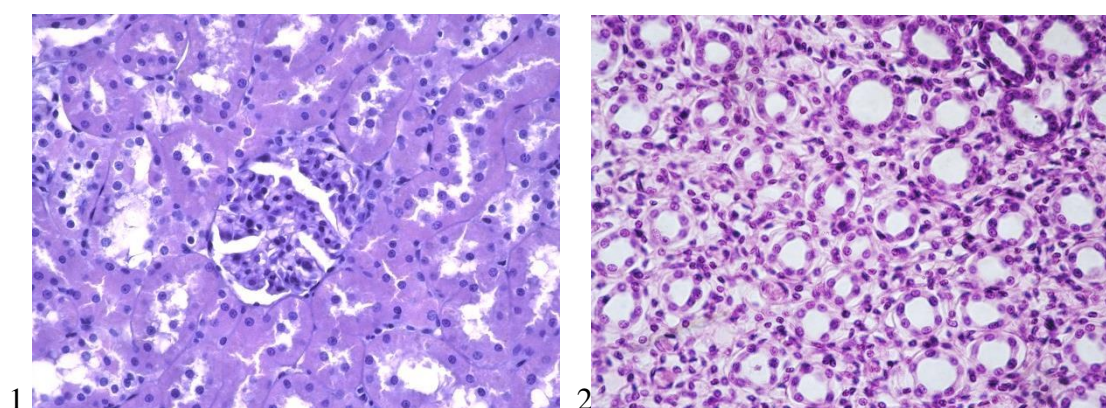


Fig. 1. Sensomotor region of the cerebral cortex of the control and experimental groups of the rats.

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

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.



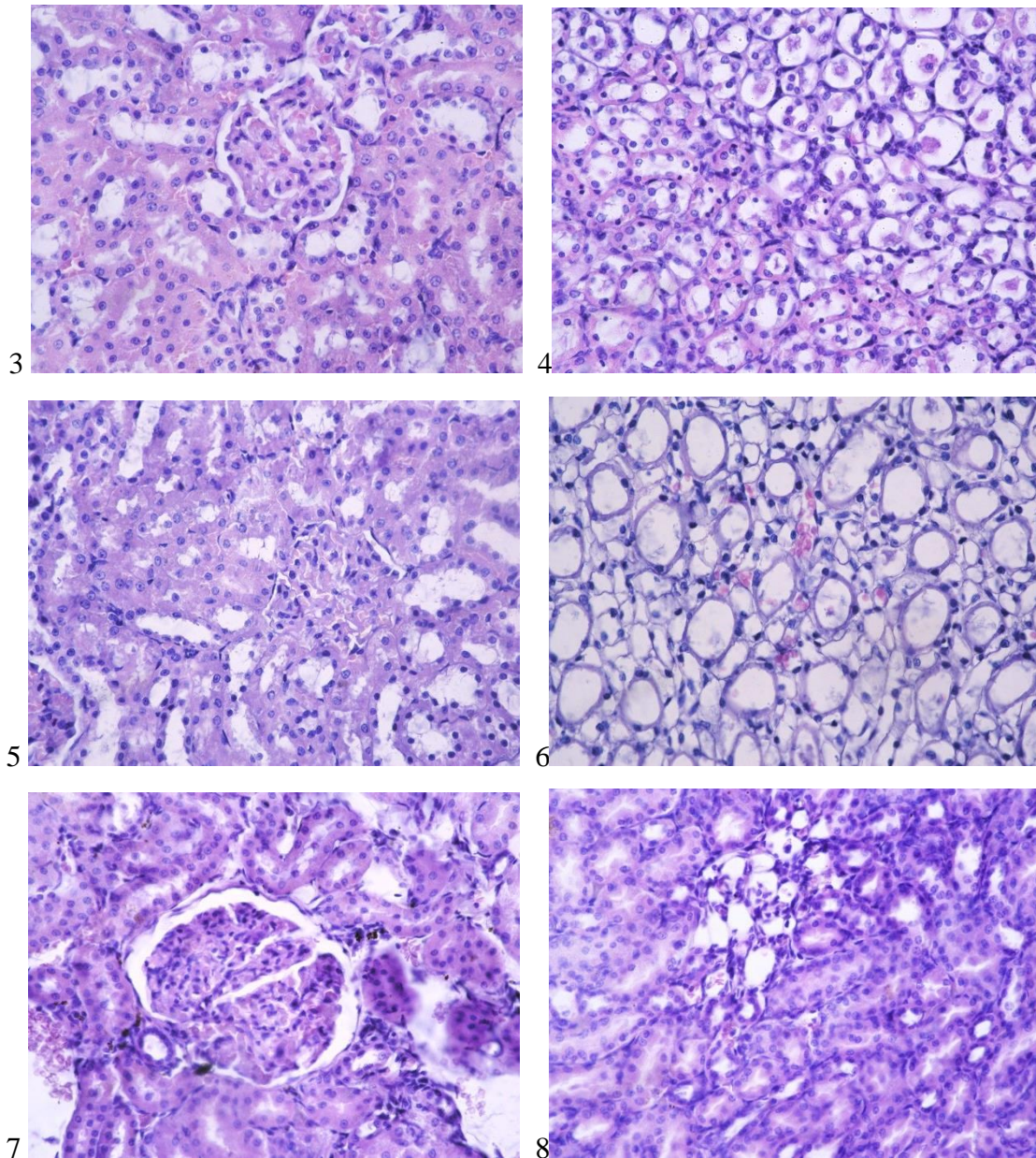


Fig. 2. The results of the histological examination of kidney of rat with hemorrhagic stroke. Structural changes of the thick tubules of the nephrons of the medulla of the kidney and of the collecting tubules of the kidney.

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, $\times 400$.

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, 3 rd day	56,9±1,58*	45,3±1,10*
3	Right kidney, 3 rd day	52,9±1,67*	49,0±1,60
4	Left kidney, 21 st day	46,9±1,22*#	36,5±0,77*#
5	Right kidney, 21 st day	51,1±1,43*	40,5±0,85*#

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

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.

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 interglomerular 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.

References

1. Tsagalis G, Akrivos T, Alevizaki M, Manios E, Stamatellopoulos K, Laggouranis A, Vemmos KN. Renal dysfunction in acute stroke: an independent predictor of long-term all combined vascular events and overall mortality. *Nephrol Dial Transplant*. 2009 Jan;24(1):194-200.
2. Power A, Stroke in Dialysis and Chronic Kidney Disease. *Blood Purif* 2013;36:179-183.
3. Covic A, Schiller A, Mardare NG, Petrica L, Petrica M, Mihaescu A, Posta N. The impact of acute kidney injury on short-term survival in an eastern european population with stroke. *Nephrol Dial Transplant*. 2008;23:2228–2234.
4. Khatri M, Himmelfarb J, Adams D, Becker K, Longstreth WT, Tirschwell DL. Acute Kidney Injury is Associated with Increased Hospital Mortality after Stroke. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2014;23(1):10.
5. Kamouchi M, Sakai H, Kiyohara Y, Minematsu K, Hayashi K, Kitazono T. Acute kidney injury and edaravone in acute ischemic stroke: the Fukuoka Stroke Registry. *J Stroke Cerebrovasc Dis*. 2013 Nov;22(8):e470-6.
6. Shametova V.G. Chronic kidney disease in patients with arterial hypertension: frequency, risk factors for development, clinical-prognostic value. — 2012. — 119 c.
7. Molshatzki N, Orion D, Tsabari R, Schwammenthal Y, Merzeliak O, Toashi M, Tanne D. Chronic kidney disease in patients with acute intracerebral hemorrhage: association with large hematoma volume and poor outcome. *Cerebrovasc Dis*. 2011;31(3):271-7.
8. Rocha R, Chander PN, Zuckerman A, Stier CT Jr. Role of aldosterone in renal vascular injury in stroke-prone hypertensive rats. *Hypertension*. 1999 Jan;33(1 Pt 2):232-7.
9. Sherifa A. Hamed, Ahmad H. Youssef, Amal M. Tohamy, Refaat F. Abd Elaal, Mahmoud M. Hassan, Eman Nasr Eldin. Acute kidney injury in patients with cerebrovascular

stroke and its relationship to short-term mortality // International Research Journal of Medicine and Medical Sciences. Vol. 3(3), pp. 70-77, July 2015

10. Tanaka M, Schmidlin O, Olson JL, Yi SL, Morris RC. Chloride-sensitive renal microangiopathy in the stroke-prone spontaneously hypertensive rat. *Kidney Int.* 2001 Mar;59(3):1066-76.