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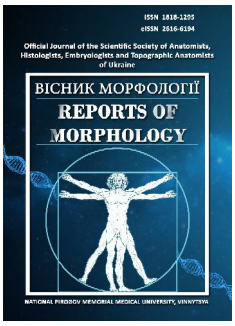

Changes in the microscopic organisation of rat adrenal glands under the influence of *Vipera berus berus* venom

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Snakebite envenoming is a common but neglected public health problem worldwide. Annual mortality as a result of snakebites exceeds 138,000. The organs of the endocrine system are among the first to react to the effects of snake and viper toxins. Under these conditions, the adrenal glands are involved in the pathological process and contribute to the formation of the adaptation syndrome, undergoing complex structural changes. The research aims to study the changes in the microscopic organization of the adrenal glands of rats under the influence of Vipera berus berus venom. Experimental studies were carried out on white non-linear male rats. The animals were conditionally divided into a control and an experimental group of 10 individuals. Experimental rats were injected intraperitoneally in a saline solution with a semi-lethal dose (LD50) (1.576 mg/g^{-1}) of Vipera berus berus venom. Animals of the control group were injected intraperitoneally with only saline solution. Rats were removed from the experiment 24 hours after exposure to the venom and anaesthetized by decapitation. Adrenal gland samples were taken for microscopic examination. Fixation of the material and preparation of paraffin blocks were carried out according to generally accepted methods. Histological preparations of the adrenal glands were stained with hematoxylin and eosin. Histological preparations were studied using an SEO SCAN light microscope. Under the influence of Vipera berus berus venom in zona glomerulosa of the adrenal cortex, moderately pronounced pathological changes were found, including vacuolization and granularity of the cytoplasm of endocrinocytes, loss of precise contours of nuclei, their hyperchromasia, expansion of lumens of sinusoidal capillaries, accumulation of erythrocytes in them. Under these conditions, zona fasciculata is characterized by significant cell granularity and perinuclear edema. Less pronounced structural organization changes were noted in the zona reticularis of the adrenal cortex. Endocrinocytes of this zone had small sizes, eosinophilic cytoplasm and dark nuclei. In the medulla of the adrenal glands, the cells were large in size and had indistinct contours, the cytoplasm was characterized by basophilic granularity, and the nuclei were light due to the predominance of euchromatin. The most pronounced effect of Vipera berus berus venom was on the zona glomerulosa and zona fasciculata of the adrenal cortex; most of the morphological signs of pathology in which were caused by a violation of protein metabolism in the cells of the parenchymal and stromal elements of this organ.

Keywords: *vipers, venom, adrenal glands, endocrinocytes, rats.*

Introduction

Snakebite envenoming is a common but neglected public health problem worldwide, especially in tropical countries. Annual mortality due to snake bites exceeds 138,000 [14, 17, 18]. It is believed that this problem is underestimated, and in many countries, individual cases of bites are not subject to proper fixation [5, 16]. In India, about 58,000 people die each year from complications caused by snake and viper venom [12, 15, 22].

About 200 species of venomous snakes are known, most of which belong to the *Elapidae* and *Viperidae* families (sometimes the *Lamprophiidae* family and the *Atractaspidinae* subfamily). They differ in the venom's chemical composition and the venomous apparatus's structure [6, 7, 8].

It is known that the toxins of snakes and vipers are a complex mixture of proteins, peptides, low molecular weight substances, and salts in the water environment [3]. Usually, the venom has a neurotoxic effect, local destruction of soft tissues in the places of its inoculation, or a vasohemotoxic effect. Clinical manifestations are diverse and include local (edema, tissue necrosis) and systemic [1, 2]. The latter manifests in neuromuscular paralysis, rhabdomyolysis, hypotension, collapse, and DIC syndrome [24, 25]. In recent years, scientists have reported the development under these conditions of endocrine and metabolic disorders due to pituitary dysfunction, adrenal gland damage, dysglycemia, electrolyte disturbances, and renal tubular acidosis [19, 20, 23].

The organs of the endocrine system are among the first to react to the effects of snake and viper toxins. The consequences of their bites can be acute or chronic in nature but cause a violation of the structure and functions of almost all central and peripheral organs of the specified system. Under these conditions, the adrenal glands are involved in the pathological process and contribute to the formation of the adaptation syndrome, undergoing complex structural changes. To date, the histological changes of the adrenal glands in the case of snake and viper bites are not sufficiently covered in the available scientific sources. In addition, there is a complete lack of data on morphological changes in the organ's structure under conditions of poisoning with toxins of the most common European vipers, namely *Vipera berus berus*, which determines the relevance of the chosen topic.

The aim of the research is to study the changes in the microscopic organization of the adrenal glands of rats under the influence of *Vipera berus berus* venom.

Materials and methods

Experimental studies were carried out on white non-linear male rats. For preliminary acclimatization, the animals were kept for seven days in the animal facility of Taras Shevchenko National University of Kyiv. Then they were kept in laboratory conditions at constant temperature (22±3°C), humidity (60±5 %) and light (12 h light/12 h dark cycle), being fed standard rodent food and water *ad libitum* [9]. All experiments were conducted by the National Institutes of Health Guidelines for the Care and Use of laboratory animals and the European Council Directive of 24 November 1986 for the Care and Use of Laboratory Animals (86/609/EEC). The research was approved and confirmed by the Bioethics Commission of the NSC "Institute of Biology and Medicine" of the Taras Shevchenko National University of Kyiv (protocol No. 2, dated August 19, 2021).

Vipera berus berus venom was obtained from the V. N. Karazin Kharkiv National University. The lyophilized crude venom was stored at -20°C and dissolved in a saline solution immediately before the experiment.

The animals were conditionally divided into a control and an experimental group of 10 individuals. Experimental rats were injected intraperitoneally in a saline solution with a semi-lethal dose (LD50) (1.576 mg/g^{-1}) of *Vipera berus berus* venom. Animals of the control group were injected intraperitoneally with only saline solution. Rats were removed from the experiment 24 hours after exposure to the venom and anaesthetised by decapitation.

Adrenal gland samples from animals of all groups were taken for microscopic examination. The pieces were fixed in a 10 % formalin solution for one day. Further, the pieces were dehydrated in alcohols of increasing concentration and embedded in paraffin blocks. Histological preparations of adrenal glands were stained with hematoxylin and eosin [13]. Histological specimens were studied using an SEO SCAN light microscope and photo-documented using a Vision CCD Camera with a system of image output from histological specimens.

Results

When exposed to *Vipera berus berus* venom, significant changes in their typical microscopic organization were observed in the adrenal glands of experimental rats.

Zona glomerulosa of the adrenal cortex of rats exposed to *Vipera berus berus* venom shows signs of moderate pathological changes. Parenchyma cells form rounded clusters separated by stroma elements. Nuclei sometimes lose precise contours (Fig. 1A), many of them are hyperchromic, and those that retain a light color are characterized by the formation of heterochromatin lumps that often accumulate under the nucleolem. Hyperchromic nuclei, in turn, have an uneven contour with signs of the early stages of karyopyknosis, which is a logical reaction of the cell to intoxication. The cytoplasm of endocrinocytes is characterized by vacuolization; in some areas, it is stained unevenly, and it also has granularity (Fig. 1D). The presence of such granularity may be associated with proteolytic processes in the cytoplasm, which lead to the accumulation of eosinophilic lumps of protein in the cytoplasm.

Stromal elements are not subject to significant changes - fibroblast nuclei are dark and flattened, as in the control group. However, the structure of the collagen fibers of the capsule appears to be loose and has unclear boundaries of both cells and extracellular elements (Fig. 1B, 1C). Such changes are generally characteristic of the stromal elements of the adrenal cortex under negative influences. If we talk about vascularization, then in contrast to the single erythrocytes inherent in the sinusoidal capillaries of the adrenal glands of animals from the control group, zona glomerulosa from this experimental group is characterized by a cluster of aggregated erythrocytes that "clog" the lumens of the sinusoids and lead to their expansion (see Fig. 1B). The presence of hollow vacuoles is also noted in the vessel lumens. Such characteristics of the microcirculatory channel can be explained by the effect of snake venom on blood plasma proteins, which can lead to its coagulation and aggregation of formal elements.

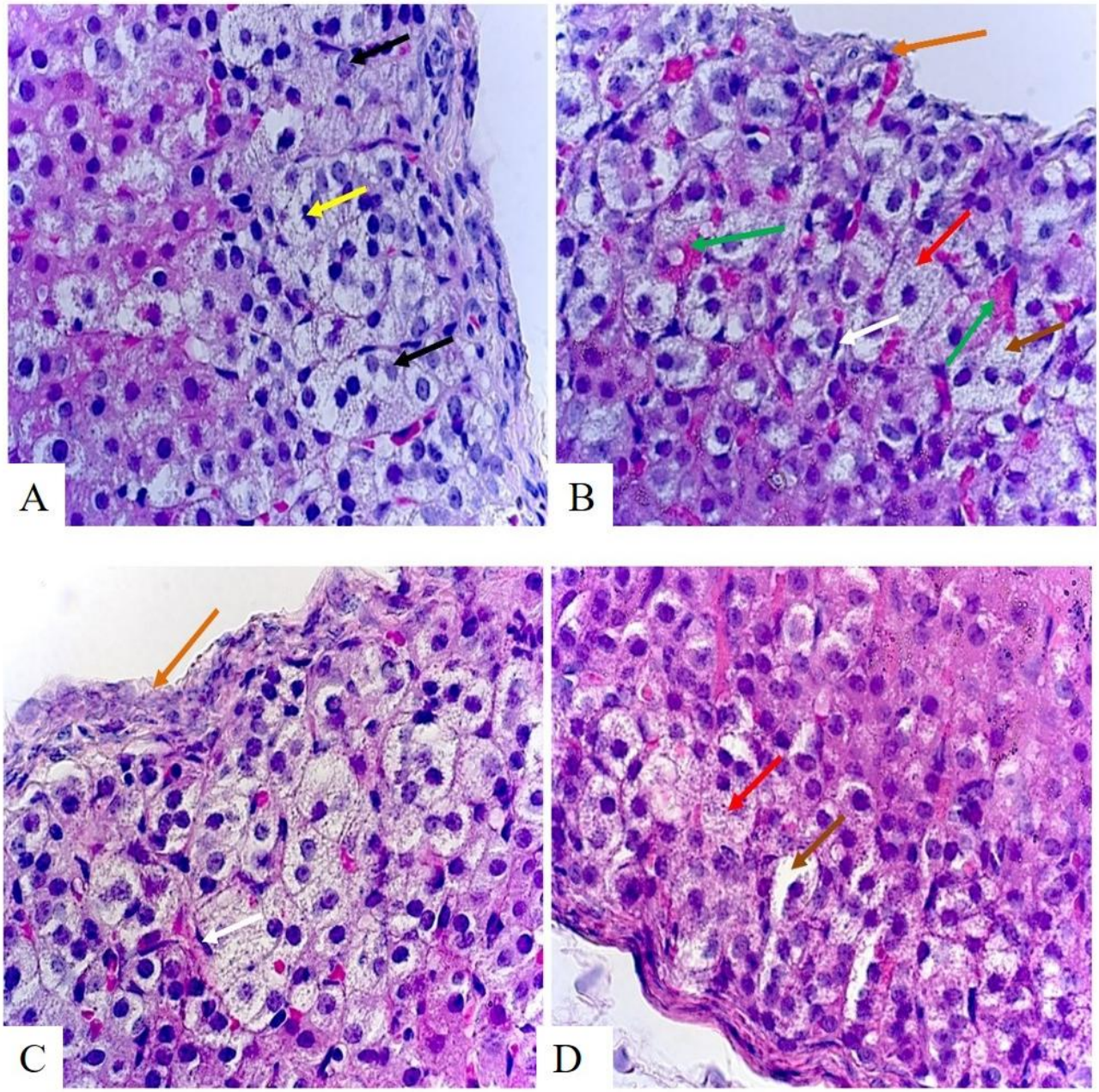

Fig. 1. Capsule and zona glomerulosa of the adrenal glands of rats from the experimental group with the injection of *Vipera berus berus* venom. A: unclear and uneven contours of nuclei (black arrows); shrunken nuclei (yellow arrows). B: accumulation of erythrocytes and vacuoles in the sinusoids (green arrows). B, C: flattened nuclei of fibroblasts (white arrows); loose collagen fibers (orange arrows). B, D: cytoplasmic vacuolization (brown arrows); cytoplasmic granularity (red arrows). Staining with hematoxylin and eosin; x1000.

Zona fasciculata of the adrenal cortex of rats from this group is characterized by columns of intensively eosinophilic cells. Their cytoplasm is characterized by pronounced granularity; cell boundaries somewhat lose clarity and become blurred. Stratification in white lumens with uneven edges on an eosinophilic background is observed in the cytoplasm, which is not the usual appearance of fat inclusions for further hormone synthesis. The number of perinuclear swellings increases; the nuclei themselves are intensively stained and have clear borders and a regular shape with smooth borders without signs of wrinkling. Quite large extracellular vacuoles are sometimes observed between the cells (Fig. 2A).

Sinusoidal capillaries in the zona fasciculata, similar to the zona glomerulosa, are filled with numerous aggregated erythrocytes, which leads to the expansion of their lumen. Single erythrocytes are challenging to distinguish, and the color of aggregated groups is uneven. Vacuoles are also sometimes observed between groups of red blood cells (Fig. 2B). The nuclei of interstitial fibroblasts remain

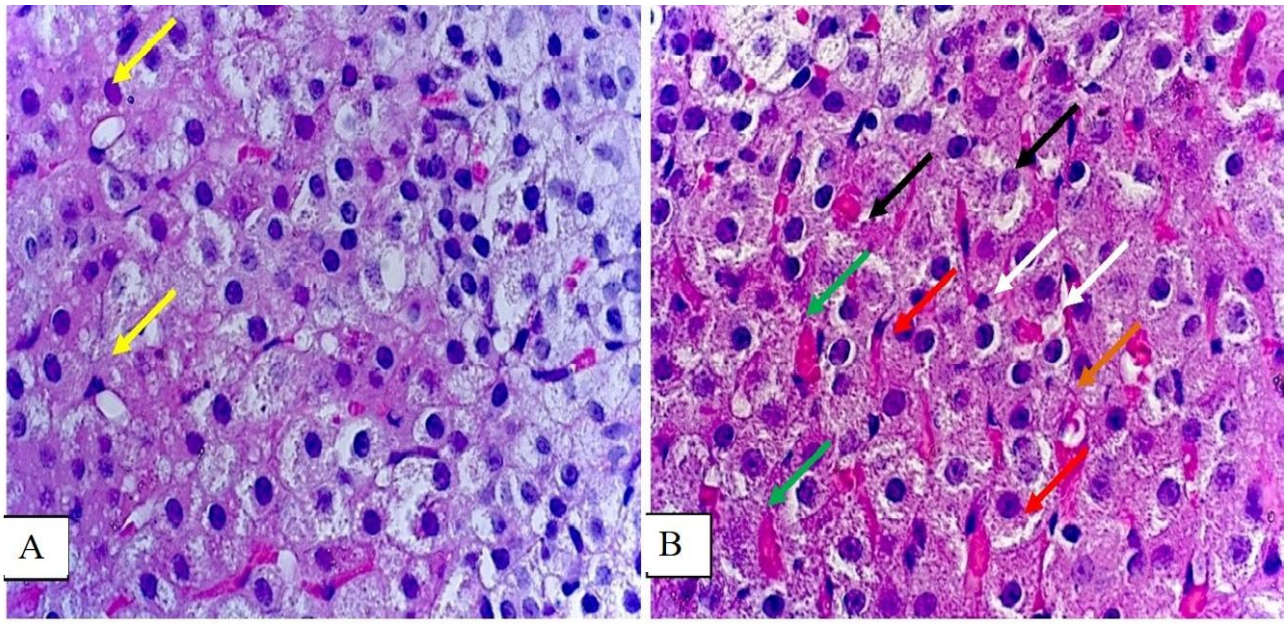

Fig. 2. Zona fasciculata of the adrenal glands of rats from the experimental group with the introduction of *Vipera berus berus* venom. A: extracellular vacuoles (yellow arrows). B: cytoplasmic granularity (red arrows); lumens in the cytoplasm (black arrows); perinuclear edema (white arrows); accumulation of erythrocytes in the sinusoids (green arrows); vacuole in the vessel lumen (orange arrow). Staining with hematoxylin and eosin; x1000.

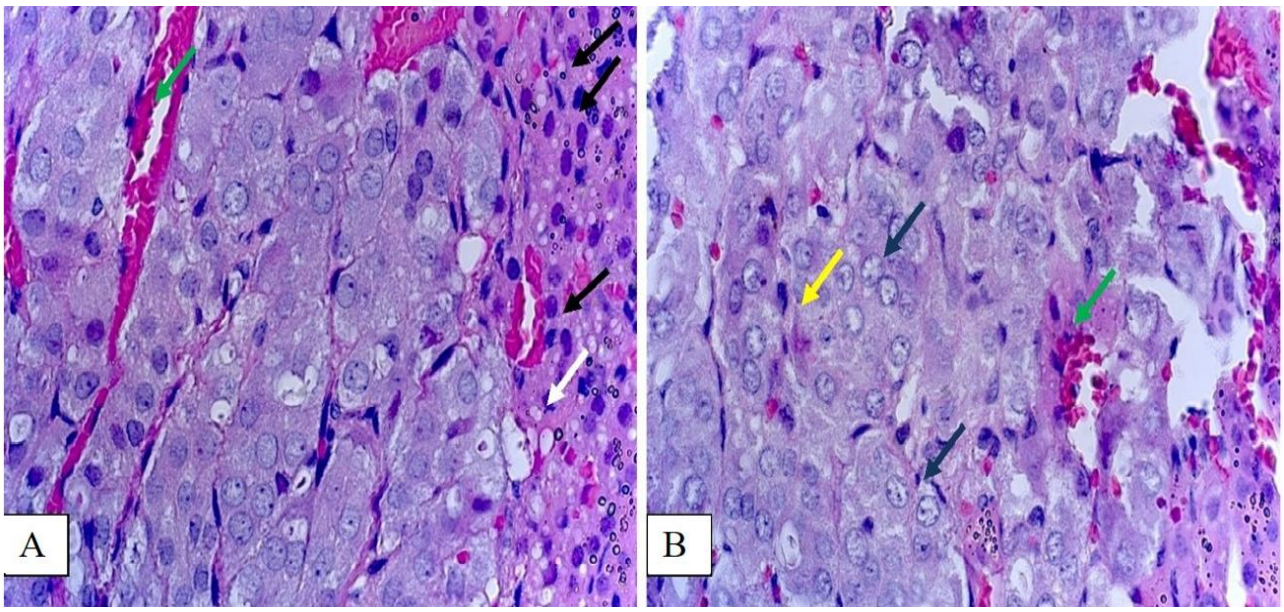

Fig. 3. Zona reticularis of the cortex (A) and the medulla (A, B) of the adrenal glands of rats from the experimental group injected with *Vipera berus berus* venom. A: elongated hyperchromic nuclei (black arrows); fat vacuole (white arrow). B: basophilic granularity (yellow arrow); euchromatic nuclei (blue arrows). A, B: vessels with aggregated erythrocytes (green arrows). Staining with hematoxylin and eosin; x1000.

flattened and dark.

Compared to other areas of the cortex of animals from this experimental group, the zona reticularis has undergone the most minor changes. Smaller sizes characterize the cells than in other zones, dark nuclei, which sometimes have an elongated shape, and eosinophilic cytoplasm with minor inclusions of fatty vacuoles (Fig. 3A, 3B).

The stroma of this zone is characterized by the presence of fibroblasts with dark, flattened nuclei, which is a typical characteristic of both other zones of the cortex of animals from this group and the control group. Dilated vessels direct to the large venous sinuses of the medulla.

Similar to the zona reticularis, the medulla of the adrenal glands does not undergo significant changes under the influence of *Vipera berus berus* venom, which is generally confirmed by the literature - the cortex reacts much more

reactively to the acute effects of poisons than the medulla. Large sizes, basophilic granularity and indistinct borders characterize the cells. The nuclei are very bright due to the predominance of euchromatin and have regular clear borders (see Fig. 3B).

The stroma of the medulla is characterized by the presence of thin interstitial connective tissue layers with elongated dark nuclei of fibroblasts and large-diameter vessels that ensure the outflow of blood from this organ, filled with formal blood elements.

Discussion

Among the known complications associated with damage of the adrenal glands in snake and viper bites are hemorrhage and acute adrenal insufficiency. Hemorrhages were recorded during numerous autopsies. In most cases, a hematoma of the adrenal glands is characteristic, and in 25 % of cases, bilateral hemorrhage was recorded, and in 6% of cases, had ischemic necrosis. Like the pituitary gland, the adrenal glands have a good blood supply, and therefore the etiology of hemorrhagic complications is equated to the Waterhouse-Friderichsen syndrome. Since the venom contains both active procoagulant components and those that cause bleeding, the development of DIC syndrome, hemorrhages and necrosis of the adrenal glands are characteristic phenomena [4].

H. J. Finol et al. [10] investigated the effect of *Bothrops venezuelensis* venom on morphological changes in the adrenal glands of experimental animals. Their results demonstrate that under these conditions, a violation of the integrity of the endothelial lining and protrusion of epithelial cells into the lumen of the capillaries were detected in the vessels of the adrenal cortex. Adrenocorticocytes contained round and oval tubular formations, which probably belonged to smooth ER. There are swollen mitochondria with a small number of crystals. Cell nuclei had vague contours enriched with heterochromatin; the perinuclear space was significantly expanded. The presence of the Golgi complex, swollen rough ER, and autophagosomes was determined. Lipid droplets with different electron densities were noticeable. Granules of lipofuscin were observed near mitochondria. 6 hours after the injection of the venom; studies showed the presence of fibroblasts with elongated nuclei in the cells of the adrenal cortex. These cells were located between the plasmalemma of adrenocorticocytes and the capillary wall. Swelling of cisterns of rough ER was detected. Mitochondria are disorganized, and lipid inclusions are visible in the cytoplasm. Chimeric formations in the cytoplasm, similar in structure to the nucleus, surrounded by a shell, were observed. Lipid inclusions had high electron density. After 24 hours of the experiment, the presence of fenestrae and individual areas with a violation of integrity were noted in the endothelial lining of the adrenal vessels. A small number of lipid droplets characterized the adrenal cortex cells, the presence of cisterns and tubules of smooth ER, numerous swollen mitochondria, multivesicular bodies, and lysosomes. In some nuclei of these cells, the perinuclear space was expanded. In some places, nuclei without heterochromatin and those containing electron-dense bodies, which probably correspond to nucleoli, were observed, but their characteristic structure was lost. The authors associate these morphological changes in the structural organization of the adrenal glands with the influence of the main components of the venom, namely proteases, PLA, and numerous non-enzymatic toxins.

According to researchers, the venom of the *Crotalus pifanorum* causes a violation of the normal histoarchitectonics of the adrenal glands of rats. It was established that 3 hours after its administration to experimental animals, swelling of mitochondrial cristae, cisterns of smooth ER, presence of Weibel-Palade bodies, and electron-dense lipid droplets are found in the cells of the organ's cortex. At the same time, individual mitochondria had tubular cristae. After 6 hours of research, capillaries were found in the cortical substance of the adrenal glands, inside which a significant number of erythrocytes were concentrated. An increase in secretory activity was observed in some endocrinocytes, manifested in an increase in organelles responsible for production and synthesis. Mitochondria had increased electron density. Lipid droplets are present in a significant amount, and smooth ER has undergone reduction. Nuclei had different electron densities and heterochromatin content, and karyolemma had signs of swelling. In some places, cells were identified where swelling or loss of mitochondrial cristae or those undergoing autophagy were observed. After 24 hours of the experiment, a violation of the structural organization of the capillary walls was detected. The latter had a detachment of the endothelium from the basement membrane. The lumen of the capillaries was filled with erythrocytes. Endotheliocytes lost the electron density of the cytoplasm; mitochondria did not have cristae. In the cytoplasm of adrenocorticocytes, there were lipid droplets, lysosomes and mitochondria with degenerative changes of the cristae. The nuclear membrane of adrenal cortex cells is swollen; degenerative processes are also visible in them. Some cells in the cytoplasm contained smooth ER and had initial signs of necrosis. It should be noted that during this study, scientists paid particular attention to structural changes in mitochondria. Thus, during their ultrastructural analysis, after 3 hours of the experiment, an increase in the intermembrane space of mitochondria, signs of their autophagy, and a violation of the integrity of the cristae were observed. In some places, there were areas of absence of the inner mitochondrial membrane. After 6 hours, organelle membrane damage and matrix vacuolization were characteristic. At the 24th hour, the research noted an even more significant expansion of the intermembrane space, an increase in the electron density of the mitochondrial matrix, ruptures, destruction of membranes, disappearance of cristae, and those

remaining cristae were swollen. The authors believe that the venom of these vipers has a toxic effect on organelles through the action of proteases and PLA [11].

Conclusions

1. Under the influence of *Vipera berus berus* venom in the zona glomerulosa of the adrenal cortex, moderately pronounced pathological changes were found, including vacuolization and granularity of the cytoplasm of endocrinocytes, loss of precise contours of nuclei, their hyperchromia, expansion of lumens of sinusoidal capillaries, accumulation of erythrocytes in them. Under these conditions, the zona fasciculata is characterized by significant cell granularity and perinuclear edema. Less pronounced structural organization changes were noted in the zona reticularis of the adrenal cortex. Endocrinocytes of this zone had small sizes, eosinophilic cytoplasm and dark nuclei.

2. In the medulla of the adrenal glands, the cells were large in size. They had indistinct contours, the cytoplasm was characterized by basophilic granularity, and the nuclei were light due to the predominance of euchromatin.

3. The venom of *Vipera berus berus* had a more pronounced effect on the zona glomerulosa and zona fasciculata of the adrenal cortex; most of the morphological signs of pathology in which were caused by a violation of protein metabolism in the cells of the parenchymal and stromal elements of this organ.

References

[1] Abd El-Aziz, T. M., Shoulkamy, M. I., Hegazy, A. M., Stockand, J. D., Mahmoud, A., & Mashaly, A. M. A. (2020). Comparative study of the in vivo toxicity and pathophysiology of envenomation by three medically important Egyptian snake venoms. *Arch Toxicol,* 94(1), 335-344. doi: 10.1007/s00204-019-02619-y

[2] Alangode, A., Rajan, K., & Nair, B. G. (2020). Snake antivenom: Challenges and alternate approaches. *Biochem. Pharmacol.,* 81, 114135. doi: 10.1016/j.bcp.2020.114135

[3] Almeida, J. R., Resende, L. M., Watanabe, R. K., Carregari, V. C., Huancahuire-Vega, S., da S Caldeira, C. A., … & Da Silva, S. L. (2017). Snake venom peptides and low mass proteins: Molecular tools and therapeutic agents. *Curr. Med. Chem.,* 4(30), 3254-3282. doi: 10.2174/0929867323666161028155611

[4] Bhattacharya, S., Krishnamurthy, A., Gopalakrishnan, M., Kalra, S., Kantroo, V., Aggarwal, S., … & Surana, V. (2020). Endocrine and metabolic manifestations of snakebite envenoming. *Am. J. Trop. Med. Hyg.,* 103(4), 1388-1396. doi: 10.4269/ajtmh.20-0161

[5] Bolon, I., Durso, A. M., Mesa, S. B., Ray, N., Alcoba, G., Chappuis, F., … & Ruiz de Castaneda, R. (2020). Identifying the snake: first scoping review on practices of communities and healthcare providers confronted with snakebite across the world. *PLoS One,* 15(3), e0229989. doi: 10.1371/journal.pone.0229989

[6] Casewell, N. R., Jackson, T. N. W., Laustsen, A. H., & Sunagar, K. (2020). Causes and consequences of snake venom variation. *Trends Pharmacol. Sci.*, 41(8), 570-581. doi: 10.1016/j.tips.2020.05.006

[7] Damm, M., Hempel, B. F., & Sussmuth, R. D. (2021). Old world vipers - a review about snake venom proteomics of viperinae and their variations. *Toxins* (Basel), 13(6), 427. doi: 10.3390/toxins13060427

[8] Di Nicola, M. R., Pontara, A., Kass, G. E. N., Kramer, N. I., Avella, I., Pampena, R., … & Paolino, G. (2021). Vipers of major clinical relevance in Europe: Taxonomy, venom composition, toxicology and clinical management of human bites. *Toxicology,* 453, 152724. doi: 10.1016/j.tox.2021.152724

[9] Dobrelia, N. V., Boitsova, L. V. & Danova, I. V. (2015). Правова база для проведення етичної експертизи доклінічних досліджень лікарських засобів з використанням лабораторних тварин [Legal basis for ethical examination of preclinical studies of drugs using laboratory animals]. *Фармакологія та лікарська токсикологія - Pharmacology and drug toxicology,* (2), 95-100.

[10] Finol, H. J., Garcia, E., Gonzalez, R., Sanchez, E. E., & Rodriguez-Acosta, A. (2020). Qualitative and quantitative ultrastructural analysis of the mitochondria from adrenal gland cortex under the action of Viperidae family snake venoms. *Int. J. Morphol.,* 38(5), 1271-1280. doi: 10.4067/S0717-95022020000501271

[11] Finol, H. J., Garcia-Lunardi, E., Gonzalez, R., Giron, M. E., Uzcategui, N. L., & Rodriguez-Acosta, A. (2020). Qualitative and quantitative study of the changes in the ultrastructure of mammalian adrenal cortex caused by the venezuelan Tigra Mariposa (Bothrops venezuelensis) snake venom. *J. Microsc. Ultrastruct.,* 8(3), 104-114. doi: 10.4103/JMAU.JMAU_49_19

[12] George, T. K., Toms, A. G., Fenn, B. N., Kumar, V., Kavitha, R., Georgy, J. T., … & Zachariah, A. (2019). Renal outcomes among snake-envenomed patients with acute kidney injury in southern India. *Natl. Med. J. India,* 32(1), 5-8. doi: 10.4103/0970-258X.272106

[13] Horalskyi, L. P., Khomych, V. T., & Kononskyi, O. I. (2011). *Основи гістологічної техніки і морфофункціональні методи досліджень у нормі та при патології [Fundamentals of histological technique and morphofunctional research methods in normal and pathology].* Житомир: Полісся - Zhytomyr: Polissya.

[14] Jayakrishnan, M. P., Geeta, M. G., Krishnakumar, P., Rajesh, T. V., & George, B. (2017). Snake bite mortality in children: beyond bite to needle time. *Arch. Dis. Child.,* 102(5), 445-449. doi: 10.1136/archdischild-2016-311142

[15] Kalita, B., Patra, A., Das, A., & Mukherjee, A. K. (2018). Proteomic analysis and immune-profiling of Eastern India Russell's Viper (Daboia russelii) venom: correlation between RVV composition and clinical manifestations post RV bite. *J. Proteome Res.,* 17(8), 2819-2833. doi: 10.1021/acs.jproteome.8b00291

[16] Longbottom, J., Shearer, F. M., Devine, M., Alcoba, G., Chappuis, F., Weiss, D. J., … & Pigott, D. M. (2018). Vulnerability of snakebite envenoming: a global mapping of hotspots. *Lancet,* 392(10148), 673-684. doi: 10.1016/S0140-6736(18)31224-8

[17] Minghui, R., Malecela, M. N., Cooke, E., & Abela-Ridder, B. (2019). WHO's snakebite envenoming strategy for prevention and control. *Lancet Glob. Health*, 7(7), 837-838. doi: 10.1016/S2214-109X(19)30225-6

[18] Paolino, G., Di Nicola, M. R., Pontara, A., Didona, D., Moliterni, E., Mercuri, S. R., … & Pampena, R. (2020). Vipera snakebite in Europe: a systematic review of a neglected disease. J. Eur. Acad. Dermatol. *Venereol.,* 34(10), 2247-2260. doi: 10.1111/jdv.16722

[19] Pucca, M. B., Knudsen, C., S. Oliveira, I., Rimbault, C., A. Cerni, F., Wen, F. H., … & Monteiro, W. M. (2020). Current knowledge

on snake dry bites. *Toxins* (Basel), 12(11), 668. doi: 10.3390/toxins12110668

[20] Seifert, S. A., Armitage, J. O., & Sanchez, E. E. (2022). Snake envenomation. *N. Engl. J. Med.,* 386(1), 68-78. doi: 10.1056/NEJMra2105228

[21] Simoes-Silva, R., Alfonso, J., Gomez, A., Holanda, R. J., Sobrinho, J. C., Zaqueo, K. D., ... & Soares, A. M. (2018). Snake venom, a natural library of new potential therapeutic molecules: challenges and current perspectives. *Curr. Pharm. Biotechnol.,* 19(4), 308-335. doi: 10.2174/1389201019666180620111025

[22] Sunil, K. K., Joseph, J. K., Joseph, S., Varghese, A. M., & Jose, M. P. (2020). Cardiac involvement in vasculotoxic and neurotoxic snakebite - a not so uncommon complication. *J. Assoc. Physicians India,* 68(11), 39-41.

[23] Ullah, A. (2020). Structure-function studies and mechanism of action of snake venom L-amino acid oxidases. *Front Pharmacol,* 11, 110. doi: 10.3389/fphar.2020.00110

[24] Variawa, S., Buitendag, J., Marais, R., Wood, D., & Oosthuizen, G. (2021). Prospective review of cytotoxic snakebite envenomation in a paediatric population. *Toxicon,* 190, 73-78. doi: 10.1016/j.toxicon.2020.12.009

[25] Waiddyanatha, S., Silva, A., Siribaddana, S., & Isbister, G. K. (2019). Long-term effects of snake envenoming. *Toxins* (Basel), 1(4), 193. doi: 10.3390/toxins11040193

ЗМІНИ МІКРОСКОПІЧНОЇ ОРГАНІЗАЦІЇ НАДНИРКОВИХ ЗАЛОЗ ЩУРІВ ПРИ ДІЇ ОТРУТИ VIPERA BERUS BERUS

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Отруєння внаслідок укусів змій є частою, але занедбаною проблемою охорони здоров'я в усьому світі. Щорічна смертність, як наслідок зміїних укусів, перевищує 138 000. Органи ендокринної системи одними з перших реагують на дію токсинів змій та гадюк. Надниркові залози за даних умов залучаються до патологічного процесу та сприяють формуванню адаптаційного синдрому, зазнаючи, однак, складних структурних перебудов. Метою дослідження є вивчення змін мікроскопічної організації надниркових залоз щурів при дії отрути Vipera berus berus. Експериментальні дослідження проводили на білих нелінійних щурах самцях. Тварин умовно розподіляли на дві групи - контрольну і дослідну по 10 особин в кожній. Дослідним щурам внутрішньоочеревинно вводили напівлетальну дозу (LD50) (1,576 мг/г$^{-1}$) отрути Vipera berus berus на фізіологічному розчині. Тваринам контрольної групи внутрішньоочеревинно вводили лише фізіологічний розчин. Виводили щурів з експерименту через 24 години після впливу отрути, знеживлюючи шляхом декапітації. Для мікроскопічного дослідження забирали зразки надниркових залоз. Фіксацію матеріалу та виготовлення парафінових блоків проводили за загальноприйнятими методиками. Забарвлення гістологічних препаратів надниркових залоз здійснювали гематоксиліном та еозином. Гістологічні препарати вивчали за допомогою світлового мікроскопа SEO SCAN. При впливі отрути Vipera berus berus в клубочковій зоні кори надниркових залоз виявлено помірно виражені патологічні зміни, серед яких вакуолізація та зернистість цитоплазми ендокриноцитів, втрата чітких контурів ядер, їх гіперхромія, розширення просвітів синусоїдних капілярів, скупчення в них еритроцитів. Пучковій зоні за даних умов притаманні значна зернистість клітин та перинуклеарний набряк. У сітчастій зоні кори надниркових відмічали менш виражені зміни структурної організації. Ендокриноцити цієї зони мали невеликі розміри, еозинофільну цитоплазму й темні ядра. В мозковій речовині надниркових залоз клітини були великих розмірів, мали нечіткі контури, цитоплазма характеризувалась базофільною зернистістю, ядра були світлими внаслідок переважання еухроматину. Найбільш виражений вплив отрута Vipera berus berus чинила саме на клубочкову та пучкову зони кори надниркових, більшість з морфологічних ознак патології в яких була спричинена порушенням білкового обміну у клітинах паренхіматозних та стромальних елементів даного органу.

Ключові слова: *гадюки, отрута, надниркові залози, ендокриноцити, щури.*