Zaiats, Liubomyr, Fedorchenko, Yuliya, Zukow, Walery. Ultrastructural organization of the respiratory part of the lungs in streptozotocin-induced diabetes. Journal of Education, Health and Sport. 2023;13(1):281-286. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2023.13.01.042
https://apcz.umk.pl/JEHS/article/view/41462
https://zenodo.org/record/7457056

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343.
Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159.
Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 15.11.2022. Revised: 15.12.2022. Accepted: 19.12.2022.

UDC:616.24+616.092.9+616.379-008.64

ULTRASTRUCTURAL ORGANIZATION OF THE RESPIRATORY PART OF THE LUNGS IN STREPTOZOTOCIN-INDUCED DIABETES

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Abstract

Background. Diabetes mellitus is a metabolic disease characterized by persistent hyperglycemia, the prevalence and incidence of which have dramatically increased worldwide. **Our research aimed** to study the dynamics of changes in the components of the respiratory part of the lungs in streptozotocin-induced diabetes. **Materials and methods.** The experiments were performed on 88 white male Wistar rats weighing 170-210 g. The animals were divided into three groups: 1 - intact (n=10); 2 - control (n=40); 3 - experimental (n=38) with a model of diabetes mellitus, which was reproduced by intraperitoneal injection of streptozotocin company "Sigma" (USA), diluted in 0.1 M citrate buffer with pH 4.5, at a rate of 60 mg/kg body weight. The control group of animals received an intraperitoneal injection with an equivalent dose of 0.1 M citrate buffer solution with a pH of 4.5.

Pulmonary tissue collection for electron microscopic examination was performed under thiopental anesthesia 14, 28, 42, and 70 days after streptozotocin injection. Pieces of lung tissue were fixed in 2.5% glutaraldehyde solution, followed by fixation in 1% osmium tetroxide solution. After dehydration, the material was poured into epon-araldite. Sections obtained on an ultramicrotome "Tesla BS-490"

were studied in an electron microscope «PEM-125K». All studies were performed under sodium thiopental anesthesia at the rate of 60 mg/kg of body weight. **Results.** Our research showed that 14 days after the modeling of streptozotocin-induced diabetes, mainly reactive changes were observed in the components of the respiratory part of the lungs. With an increase in the duration of the study (28-70 days), changes of a dystrophic-destructive nature were noted in alveolocytes of types I and II, and endotheliocytes of hemocapillaries. At the same time, cells with increased functional activity were determined in the components of the respiratory part of the lungs. **Conclusion.** Streptozotocin-induced diabetes leads to violations of the ultrastructural organization of components of the respiratory part of the lungs. The nature and severity of structural changes in type I, II alveolocytes, and endotheliocytes of hemocapillaries depend on the duration of diabetes.

Keywords: streptozotocin-induced diabetes, lungs, respiratory part.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by persistent hyperglycemia, the prevalence and incidence of which have increased dramatically worldwide [3, 5, 9, 11, 19]. Numerous clinical and experimental studies show that DM affects many organs and systems of the body [1, 8, 10, 14, 16]. Retinopathy, nephropathy, neuropathy, and cardiovascular dysfunction are common diabetic complications and contribute significantly to morbidity. However, there is increasing evidence that the lungs are also one of the target organs in DM [6, 12, 15, 17]. To date, issues related to changes in the respiratory part of the lungs (RPL) in DM have not been sufficiently studied.

The aim. To study the dynamics of changes in components of respiratory part of the lungs in streptozotocin-induced diabetes.

MATERIALS AND METHODS

The experiments were performed on 88 white male Wistar rats weighing 170-210 g, which were kept on a standard diet with free access to water. Animals were divided into three groups: 1 - intact (n=10); 2 - control (n=40); 3 - experimental (n=38) with a model of DM, which was reproduced by intraperitoneal injection of streptozotocin company "Sigma" (USA), diluted in 0.1 M citrate buffer with pH 4.5, at a rate of 60 mg/kg body weight. An equivalent dose of 0.1 M citrate buffer solution with a pH of 4.5 was intraperitoneally injected to the control group of animals.

Pulmonary tissue collection for electron microscopic examination was performed under thiopental anesthesia 14, 28, 42, 70 days after streptozotocin administration. Pieces of lung tissue were fixed in 2.5% glutaraldehyde solution, followed by fixation in 1% osmium tetroxide solution. After dehydration, the material was poured into epon-araldite. Sections obtained on an ultramicrotome «Tesla BS-490» were studied in an electron microscope «PEM-125K». All studies were performed under thiopentalone sodium analgesia at a rate of 60 mg/kg body weight.

Animal husbandry and research were conducted in accordance with the provisions of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), the Law of Ukraine on the "Protection of Animals from Cruelty" (2006) and the "General Ethical Principles of Experiments on animals" approved by the Fifth National Congress on Bioethics (Kyiv, 2013).

RESULTS AND DISCUSSION

The conducted ultrastructural analysis showed that 14 days after the start of the experiment, the nuclei of alveolocytes of type I (A-I), type II (A-II) and endotheliocytes of hemocapillaries mainly had a matrix of medium electron-optical density and an even distribution of chromatin granules over the entire area of the nucleus. Cell organelles were without particular structural changes. In separate endotheliocytes, slightly expanded tubules of the rough endoplasmic reticulum (RER) were noted. An increased number of micropinocytotic vesicles was observed in the peripheral sections of endothelial cells.

With an increase in the duration of the study (28 days), the cytoplasm of A-I, A-II and endotheliocytes was with a fine-grained matrix and marginal aggregation of chromatin granules. The nuclear envelope had tortuous contours and formed shallow intussusceptions. The perinuclear space was slightly expanded. In many cases, the mitochondria of these cells were swollen with single cristae. The cisterns and tubules of the Golgi apparatus (GA) and RER were moderately expanded. The marginal folds of anucleated areas of cytoplasm protruding into the lumen of microvessels were defined on the lumenal surface of some endotheliocytes. In the peripheral area of endothelial cells, an increased number of small and large micropinocytotic vesicles was found, which often merged to form large vacuoles. In the lumen of some hemocapillaries, we observed red blood cell aggregates, adhesion and aggregation of white blood cells and platelets.

The results of submicroscopic studies performed in 42-70 days indicated pronounced violations of the ultrastructural organization of the components of the respiratory part of the lungs. Alterations in the cells of the alveolar epithelium and endotheliocytes were accompanied by the development of intracellular edema with a violation of the structure of organelles (fig.).

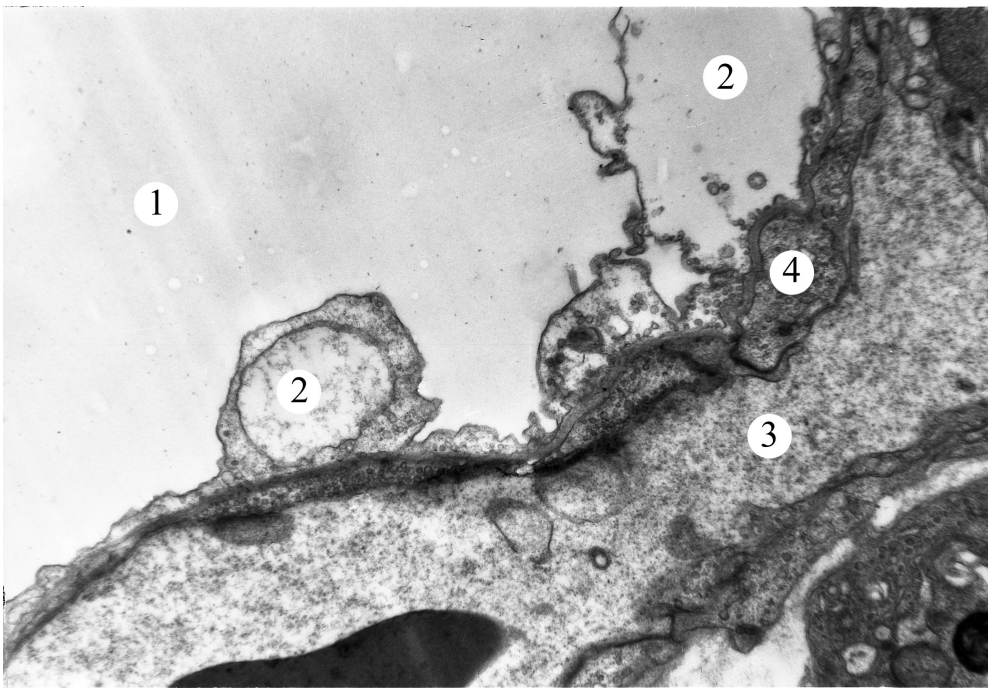

Fig. 1. Ultrastructural organization of the respiratory part of the lungs 42 days after the start of the experiment. Electronic microphotography x6400

Marking: 1 – lumen of the alveoli; 2 – type I alveolocyte; 3 – hemocapillary lumen; 4 – endotheliocyte.

Mitochondria of cells were swollen with individual disorganized cristae. Constituent components of GA and RER were expanded and fragmented. The number of ribosomes on the outer surface of RER membranes was significantly reduced. In A-II part of lamellar bodies was deformed, partially filled with phospholipid material with disorganized and fragmented plates. In the lumen of the hemocapillaries of the alveolar wall, red blood cell sludge, adhesion and aggregation of white blood cells and platelets were observed. In some hemocapillaries, a violation of the integrity of the lumenal plasmolemma was noted.

Our research showed that 14 days after streptozotocin-induced diabetes modeling, mainly reactive changes were observed in the components of the respiratory part of the lungs. With an increase in the duration of the study (28-70 days), changes of dystrophic-destructive nature were noted in alveolocytes of types I and II, and endotheliocytes of hemocapillaries. At the same time, individual cells with increased functional activity were identified in the components of the respiratory part of the lungs.

The data we obtained are consistent with the results of research by a number of scientists who studied the ultrastructural organization of the components of the RPL under the influence of various endogenous factors [2, 4, 7, 13, 18].

CONCLUSIONS

1. Streptozotocin-induced diabetes leads to violations of the ultrastructural organization of the components of the respiratory part of the lungs.

2. The nature and severity of structural changes in type I, II alveolocytes, and hemocapillaries of endotheliocytes depend on the duration of diabetes.

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