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THE EFFECT OF HYPOXIA ON THE MORPHOLOGICAL AND FUNCTIONAL QUALITIES OF THE INTERALVEOLAR CAPILLARIES OF THE LUNGS AFTER ACUTE PHYSICAL LOAD IN THE EXPERIMENT

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The purpose the study was a comprehensive study of the structural restructuring of the respiratory section of the lungs during physical exertion in the experiment, the determination of the morphological equivalent of acute fatigue of the air-blood barrier. The study was performed on 30 laboratory-outbred male rats weighing 120.0–150.0 g. Histological and electron-microscopic methods were used. Experimental findings once again prove that alveolar hyperventilation affects respiratory alveolocytes and the endothelium of interalveolar capillaries, predetermining the further course of the pathological process in the aero-hematic barrier. Analysis of the available factual data on the submicroscopic reorganization of the endothelium in the early stages of hypoxia will allow us to agree with the opinion about deep violations of the pulmonary capillaries during acute limiting physical activity. An increase in the permeability of the alveolar-capillary membrane, pulmonary vascular resistance, and a violation of the mechanics of breathing with the development of alveolar hypoxia is currently recognized as the main pathogenic factors of hypoxemia and damage to the lung parenchyma.

Key words: physical load, interalveolar capillaries, hypoxia, acidosis.

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ВПЛИВ ГІПОКСІЇ НА МОРФОФУНКЦІОНАЛЬНІ ЯКОСТІ МІЖАЛЬВЕОЛЯРНИХ КАПІЛЯРІВ ЛЕГЕНЬ ПІСЛЯ ГОСТРОГО ФІЗИЧНОГО НАВАНТАЖЕННЯ В ЕКСПЕРИМЕНТІ

Метою дослідження було комплексне вивчення структурної перебудови респіраторного відділу легень при фізичному навантаженні в експерименті, визначення морфологічного еквівалента гострої втоми аерогематичного бар'єру. Дослідження виконано на 30 лабораторних безпородних щурах-самцях масою 120,0–150,0 г. Використовували гістологічні та електронно-мікроскопічні методи. Результати експерименту ще раз доводять, що альвеолярна гіпервентиляція вражає дихальні альвеолоцити та ендотелій міжальвеолярних капілярів, зумовлюючи подальший перебіг патологічного процесу в аерогематичному бар'єрі. Аналіз наявних фактичних даних щодо субмікроскопічної реорганізації ендотелію на ранніх стадіях гіпоксії дозволить погодитися з думкою про глибокі порушення легеневих капілярів при гострому обмеженні фізичного навантаження. Основними патогенними факторами гіпоксемії та ушкодження паренхіми легень у цей час визнано підвищення проникності альвеолярно-капілярної мембрани, легеневого судинного опору та порушення механіки дихання з розвитком альвеолярної гіпоксії.

Ключові слова: фізичне навантаження, міжальвеолярні капіляри, гіпоксія, ацидоз.

The respiratory system includes the airways, the respiratory section, and the motor apparatus. Each of them is an independent section with a special structure, function, and regulation, the study of which is devoted to numerous monographs, manuals, and reviews [1, 2, 7, 11, 14].

We will turn to some parts of this system, in particular the respiratory department, which provides blood transport and gas exchange through the alveolar-capillary membrane.

These processes are commonly referred to as ventilation, perfusion, and diffusion. However, before oxygen molecules acquire the ability to be involved in the terminal oxidation reaction in mitochondria and interact with ionized hydrogen, they have to overcome the system of semipermeable biological membranes that transport oxygen from the alveolar air to the mitochondrial matrix.

The lungs are not just a reservoir of blood; the capacity of the lungs' arterial, capillary, and venous beds is regulated by both extrapulmonary and local factors. Local reflective reactions are stimulated by hypoxia and acidosis, which can directly affect the vascular system.

There are many controversial issues, the study of which requires the use of a comprehensive methodological approach to analyze morphological changes at the level of hepatoparenchymal barriers and ultrastructure.

The purpose of the study was to establish the structural restructuring of the respiratory section of the lungs during physical exertion in the experiment and to determine the morphological equivalent of acute fatigue of the aero-hematic barrier.

Materials and methods. The study was performed on 30 laboratory-outbred male rats weighing 120.0-150.0 g, of which 6 were controls. Physical activity was carried out by random running on a rotating wheel (Vop=20 rpm) 2 hours after the first feeding. Wheel diameter: 0.5m. Humidity in the chamber: 59 %. Daily cycle 12/12. Before and at the end of the experiment, the behavior of the animals was recorded. Attention was paid to the state of the conjunctiva, hairline, reaction to sound, the approach of the experimenter, etc. The following indicators of fatigue were considered: adynamia, exophthalmos, and epistaxis.

Animals were subjected to a single physical activity until complete fatigue (running for 3 hours).

The object of the study was the lungs of rats. The study of the lungs was carried out by histological, histochemical, and electron microscopic methods. For light-optical examination, 5–6 pieces were taken from both lungs from the central, deep, and subpleural areas. The material was fixed in 12 % formalin and Carnoy's Solutions and embedded in paraffin.

For a general morphological study of the lungs, paraffin sections 5-8 μm thick were stained with hematoxylin and eosin and picrofuchsin according to the Van Gieson method.

Two methods of fixation were used for electron microscopy: immersion and perfusion.

For immersion fixation, pieces taken from the central and peripheral parts of both lungs were fixed in a 2 % solution of osmic acid (OsO_4) prepared in cacodylate buffer (pH = 7.34–7.41) for 2 hours.

In another group of animals, perfusion was performed through the pulmonary artery with a mixture of 2.5 % glutaraldehyde and 4 % paraformaldehyde according to the method of Karnovsky M. (1965). The above solutions were prepared in 0.1 M phosphate buffer (pH = 7.2–7.4). After perfusion, tissue samples were fixed in a 2 % osmic acid solution for 1.5–2 h on ice. After the end of fixation, the pieces were washed twice. Dehydration was carried out at alcohol concentrations and absolute acetone. Polymerization was carried out on a thermostat for 48 hours at a temperature of 58°C.

Semi-thin and ultra-thin sections were prepared on a Reichert OM-U3 ultramicrotome using glass knives. Ultrathin sections were stained by double staining with uranyl acetate and lead citrate. The study was carried out on a Tesla BS 500.0 electron microscope at an accelerating voltage of 70 kV.

The thickness of the aero-hematic barrier (AHB) was determined with a final increase of X 18,000 in the core. The technique proposed by Weibel E. (2001) was used.

The obtained digital data were subjected to statistical processing using the method of medical statistics. Further, to verify and refine the results obtained, a nonparametric criterion U, the Wilcoxon (Mann-Whitney) criterion, was used. The calculations were carried out on a computer using an Excel spreadsheet.

Research work on animals was carried out at the Scientific Research Center of the Azerbaijan Medical University in accordance with the ethical rules specified in Protocol No. 31 of the ethics rules Commission and Bioethics Committee under the Ministry of Health of the Republic of Azerbaijan on 21.04.2008.

Results of the study and their discussion. An autopsy of the animals revealed distinct macroscopic changes in the lungs in the form of focal hemorrhages of various sizes, from small punctures to those reaching 2–3 cm in diameter. Hemorrhages were located subpleural and in the depth of the parenchyma but prevailed in the lower lobes of both lungs. Blood and mucus in the trachea and bronchi were found.

An electron microscopic examination of the lungs showed that early changes in them are intimately related to the state of the capillary ultrastructure.

Closely related to the mechanics of respiration, this physiological mechanism becomes pathological in alveolar hypoxia due to a decrease in pO_2 in the inhaled air.

The nature of the task posed in our study determines the special interest in the question of the morphological assessment of the state of pulmonary blood flow with an increase in the body's need for oxygen.

This also explains the need to consider the electron microscopic picture of the lungs simultaneously, taking into account all the components of the aero-hematic barrier. The reflective expansion of the existing capillaries and the opening of new ones that were previously in a dormant state explain the increase in the functional activity of the endothelium of the alveolar capillaries noted by electron microscopic examination. Hypoxemia can also occur during normal ventilation if the diffusion of oxygen from the alveoli into the blood of the pulmonary capillaries is difficult.

In the early stages, the most common are violations of the microcirculatory bed, namely capillaries, which are component parts of the air-blood barrier. In comparison to the "conditional norm" image, the ultrastructure of the interalveolar capillaries has altered.

First, the irregularity of the lumen of interalveolar capillaries was noted. The universal sign of a change in the air-blood barrier during an acute experiment was an increase in the permeability of all its elements, diffuse edema, and an increase in vesicular and vacuolar components in the alveolar epithelium and capillary endothelial cells.

Alveolar hypoxia and hypoventilation, which result in hypercapnia and an uneven distribution of blood in the lungs, contribute to dystrophic-destructive changes in the interalveolar capillaries and indicate a change in the capillary ultrastructure already two hours after the end of the load, creating unfavorable conditions for capillary hemodynamics.

In our experiments, capillaries with a narrowed lumen are noted due to swelling of the perikaryon or due to the appearance of long cytoplasmic protrusions with a sharply edematous, swollen matrix (Fig. 1). Here it is appropriate to note that this transformation occurred in many capillaries of the subpleural and central parts of the lungs, which allows us to speak about the violation of hemocirculation in these areas.

Endothelial cells are almost devoid of their characteristic organ-specific thinning. The number of organelles is reduced; mitochondria with a swollen, vacuolated matrix are often recorded, while the organelles are concentrated not only in the perinuclear zone, as in the control, but also in the marginal parts of the cell.

Significant changes were found in the basal layer of capillaries in the lungs of rats during acute fatigue. The non-cellular component is edematous; however, in some places, it has an uneven density and width, and sometimes it is sharply drained and interrupted. In areas where there is significant enlightenment of the precapillary zone, the non-cellular component of the basal layer is loosened and expanded. The boundaries of the basal layer lose their external clarity and loosen, sometimes in the form of a border. Although individual fibrils can be differentiated, in those places where the basal layer merges with the lining of the same name, both layers have fuzzy contours (Fig. 2).

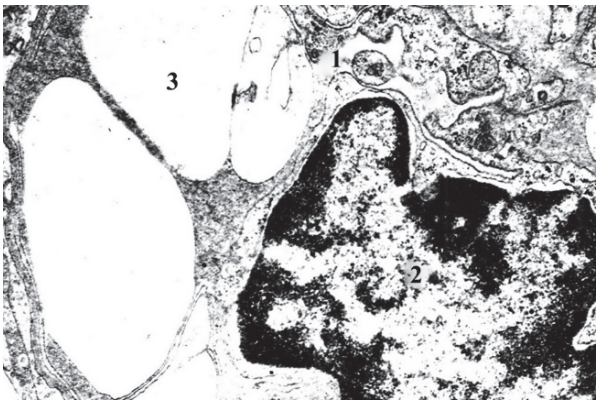

Fig.1. Acute load. The lung of a young adult rat. Magnification x18000. Note*:* 1 – interalveolar capillary with a narrowed lumen; 2 – swelling of the perikaryon of the endothelial cell; 3 – large vacuoles in the cytoplasm.

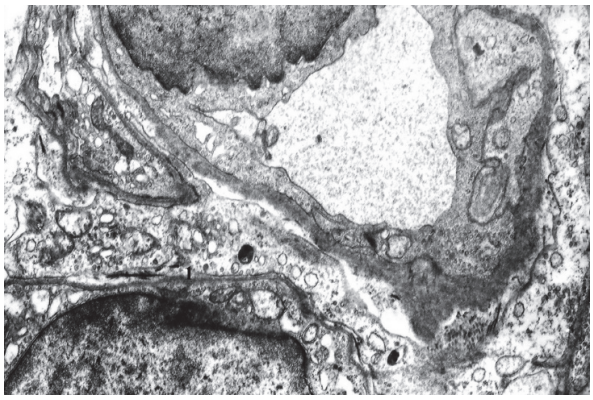

Fig. 2. Acute load. The lung of a rat, magnification x 12000. Note*:* 1 – uneven configuration and homogenization of non-cellular components of the basal layer of capillaries, loss of clarity at the points of confluence with the layer of the alveolar epithelium.

It should be noted that different degrees of change can be observed in the same capillary, which indicates the heterogeneity of the reaction of the capillary wall.

However, information on the dynamics of restructuring of various structural elements of the respiratory part of the lungs under stress-induced hypoxia, taking into account the cellular mechanisms of these changes, is not sufficiently presented in the literature. Of interest are those works that are devoted to the search for means and mechanisms for restoring impaired function [1, 2, 3, 7].

In response to the influence of various exo- and endogenous factors, structural and functional rearrangements occur, which are used by the body to develop compensatory and adaptive reactions [1–12].

After acute extreme physical load to the point of fatigue, according to our data, a spasm of small bronchi and bronchioles was detected in the respiratory part of the respiratory system, and in larger bronchi, acute hypoxia caused hyperemia and swelling of the mucous membrane with a picture of hypersecretion. In the capillaries of the interalveolar septa, aggregation of erythrocytes and sludge phenomena were constantly observed. These data on increased permeability of the vascular and bronchioles walls correspond to literature data [7, 8, 14]. In our material, in addition to a swelling of the walls of the respiratory

bronchioles, a sharp infiltration of lymphocytes and neutrophils was noted, which we explained by an increase in the permeability of the walls.

According to Tsagareli ZG, Gogiashvili LE, Topuria ZM, and Dzhandieri KN [14], in the case of a decrease in the permeability of the alveolar-capillary membrane, pulmonary ischemia develops, the production of surfactant decreases, due to which atelectasis develops, a deterioration in the blood circulation of the lungs and, accordingly, the trophism of alveolocytes becomes inevitable. It is of interest to compare the data from our experiments with the data of the above authors. In particular, after a one-time extreme physical load, attention is drawn to an increase in the permeability of all components of the airborne barrier, diffuse swelling (including stroma), an increase in the number of vesicular and vacuolar components in the cells of the alveolar epithelium and capillary endothelium. The lumens of the interalveolar capillaries were uneven, and their permeability increased, which contributed to the process of leukocyte migration.

In our experiments, after acute physical load, dramatic changes were observed in hypoventilated areas of the lungs caused by pulmonary ischemia induced by vasospasm. It is known that the alveoli are nourished by the same capillaries that carry out gas exchange. The pulmonary arterial vessels provide all the functions of the alveolar tissue, while the bronchial vessels provide the functions of the respiratory tract. The existence of anastomoses between them at the level of terminal bronchioles has been proven. Based on the above, it is clear that there are separate atelectasis areas in the lung tissue after acute extreme physical activity and, accordingly, the changes noted in type II alveolocytes after prolonged physical activity were more pronounced. In particular, in our material, after acute fatigue in areas of atelectasis, type II alveolocytes were swollen and increased in size.

In our experimental material, the vascular spasm was clearly expressed, in particular after acute physical stress, mainly in small vessels, and after prolonged physical activity, vessels of almost all calibers, both arterial and venous, were sharply narrowed. Furthermore, we noted thickening walls of small arteries (at the level of terminal bronchioles) and the disappearance of muscle elements in small veins.

In our case, after acute physical activity in the fatigue mode, spasm of small arteries and congestion of capillaries are replaced after chronic physical activity by narrowing of the lumen of the veins, atrophy of their walls due to thinning of the intima, and in small arteries, thickening of the elastic membrane. Under acute lung load, irregular capillary wall alterations reflecting their uneven functional activity in various zones were observed. One of the possible causes of mosaicity for both normal and pathological conditions is the mechanism of expiratory closure of the airways, the so-called “airway closure”, “gas trapping”, etc. [10–14].

Thus, experimental observations once again prove that alveolar hyperventilation affects respiratory alveolocytes and the endothelium of interalveolar capillaries, predetermining the further course of the pathological process in the AHB.

Conclusion

Analysis of the available factual data on the submicroscopic reorganization of the endothelium in the early stages of hypoxia will allow us to agree with the opinion about deep violations of the pulmonary capillaries during acutely limiting physical activity.

An increase in the permeability of the alveolar-capillary membrane, pulmonary vascular resistance, and a violation of the mechanics of breathing with the development of alveolar hypoxia is currently recognized as the main pathogenic factors of hypoxemia and damage to the lung parenchyma.

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EXPERIMENTAL SUBSTANTIATION OF PREVENTION OF BONE METABOLISM DISORDERS IN THE JAWS OF RATS UNDER EXPERIMENTAL PERIODONTITIS BECAUSE OF ALIMENTARY VITAMIN D DEFICIENCY

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The purpose of this study was to investigate the efficacy of prevention of remodeling disorders in the bone tissue of the alveolar process of the rat jaws with periodontitis against the background of alimentary deficiency of vitamin D. The experimental study was conducted on 36 white Wistar rats of both genders (1 month old, weight 100±5 g), which were divided into 3 groups. The degree of atrophy of the alveolar process was assessed. The activity of elastase, acid phosphatase, alkaline phosphatase, calcium and phosphorus content was determined in the homogenates of jaw bone tissue. The result of the analysis indicates the prevalence of osteoresorption processes over osteosynthesis. The proposed therapeutic and prophylactic complex showed a periodontal protective effect, which was formed due to its properties to increase the activity of alkaline phosphatase, calcium and phosphorus content against the background of a decrease in acid phosphatase and elastase in the bone tissue of the rat alveolar processes modeled with alimentary D-deficient periodontitis.

Key words: experiment, rats, vitamin D deficiency, periodontitis, biochemical parameters, bone metabolism.

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ЕКСПЕРИМЕНТАЛЬНЕ ОБГРУНТУВАННЯ ПРОФІЛАКТИКИ ПОРУШЕНЬ МЕТАБОЛІЗМУ КІСТКОВОЇ ТКАНИНИ ЩЕЛЕП ЩУРІВ ПРИ ЕКСПЕРИМЕНТАЛЬНОМУ ПАРОДОНТИТІ НА ТЛІ АЛІМЕНТАРНОГО ДЕФІЦИТУ ВІТАМІНУ D

Метою цієї роботи було дослідження ефективності профілактики порушень ремоделювання у кістковій тканині альвеолярного відростка щелеп щурів з пародонтитом на тлі аліментарного дефіциту вітаміну D. Експериментальне дослідження було проведено на 36 білих щурах лінії Wistar обох полів (1 місяць, маса 100±5 г), яких поділили на 3 групи. Оцінювали ступінь атрофії альвеолярного відростка. У гомогенатах кісткової тканини щелеп визначали активність еластази, кислої фосфатази, лужної фосфатази, вміст кальцію та фосфору Результат аналізу вказує на превалювання процесів остеорезорбції над остеосинтезом. Запропонований лікувально-профілактичний комплекс виявив пародонтопротекторну дію, яка формувалась завдяки його властивостям підвищувати активність лужної фосфатази, вмісту кальцію та фосфору на тлі зниження кислої фосфатази та еластази в кістковій тканині альвеолярних відростків щурів, яким моделювали аліментарний D-дефіцитний пародонтит.

Ключові слова: експеримент, щури, дефіцит вітаміну D, пародонтит, біохімічні показники, метаболізм кісткової тканини.

The work is a fragment of the research project "Improving the diagnosis and treatment of diseases of the oral mucosa in people with chronic somatic diseases", state registration No. 0119U003571.

Micronutrient deficiency or "hidden hunger" is a global health problem that affects more than 2 billion people worldwide [11]. In recent decades, more and more attention has been paid to vitamin D and its relationship with various diseases. Vitamin D deficiency affects more than 80 % of children in developed countries, even in countries with sufficient sunlight [10]. Vitamin D plays a crucial role in the prevention of rickets associated with its deficiency, supports optimal bone health, muscle strength, and