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STRUCTURAL CHANGES OF THE RESPIRATORY ORGANS DUE TO COVID-19 DISEASE

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✓ ***Resume***

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has reached pandemic levels. There is now ample evidence that COVID-19 can seriously affect the heart, blood vessels, nerves, brain, kidneys, and skin. Of course, the lungs and airways are the focus of COVID-19 respiratory disease. This article examines the literature on structural (morphological and hemodynamic) changes in the lungs against the background of COVID-19. The main disorders in this case were associated with a violation of pulmonary hemodynamics at the level of the pre- and post-capillary bed and were determined by the severity of signs of blood filling of the vessels, increased pressure in them, the level of congestion and permeability of the vascular walls, especially in the venous area.

Keywords: COVID-19, lung morphology, pulmonary edema, lungs, stress factors, immobilization, hypothermia, pulmonary circulation, cardiorespiratory system, rheogram

СТРУКТУРНЫЕ ИЗМЕНЕНИЯ ДЫХАТЕЛЬНЫХ ОРГАНОВ ПРИ ЗАБОЛЕВАНИИ COVID-19

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✓ ***Резюме***

Тяжелый острый респираторный синдром коронавирус 2 (SARS-CoV-2), вызывающий коронавирусную болезнь 2019 г. (COVID-19), достиг пандемического уровня. В настоящее время имеются многочисленные свидетельства того, что коронавирус COVID-19 может серьезно поражать сердце, кровеносные сосуды, нервы, мозг, почки и кожу. Конечно, легкие и дыхательные пути находятся в центре внимания при респираторном заболевании COVID-19. В данной статье изучена литература, посвященная структурным (морфологические и гемодинамические) изменениям лёгких на фоне COVID-19. Основные нарушения при этом были связаны с нарушением легочной гемодинамики на уровне пре- и посткапиллярного русла и определялись степенью выраженности признаков кровенаполнения сосудов, повышения давления в них, уровня застойных явлений и проницаемости сосудистых стенок, в особенности на венозном участке.

Ключевые слова: COVID-19, морфология легких, отек легких, легкие, стресс-факторы, иммобилизация, гипотермия, легочное кровообращение, кардиореспираторная система, реограмма.

COVID-19 КАСАЛЛИГИДА НАФАС АЪЗОЛАРИНИНГ СТРУКТУРАВИЙ ЎЗГАРИШЛАРИ

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✓ ***Резюме***

Кучли ўткир респиратор синдром коронавирус 2 (SARS-CoV-2), коронавирус касаллигини келтириб чиқаради. COVID-19 2019-йилда пандемия даражасига етди. Ҳозирги вақтда COVID-19 коронавируси юрак, қон томирлари, асаб, буйрак ва терига жиддий таъсир кўрсатиши мумкинлиги ҳақида кўплаб далиллар мавжуд. Албатта, ўпка ва нафас олиш йўллари COVID-19 да кенг тарқалганлиги, кўплаб асоратларга олиб келганлиги сабаб диққат марказида. Ушбу мақолада COVID-19 фонида ўпкада структур (морфологик ва гемодинамик) ўзгаришлар ҳақида адабиётлар кўриб чиқилган. Бундай ҳолда асосий бузилишлар ўпка гемодинамикасининг пре- ва посткапилляр тизим даражасида бузилиши билан боғлиқ бўлиб, томирларнинг қон билан тўлишишнинг бузилиши, улардаги босимнинг ошиши, томир деворларида димланиш белгиларининг турғунлиги, айниқса, веноз тизимида бу ўзгаришларнинг яққоллиги билан аниқланади.

Калит сўзлар: СОВИД-19, ўпка морфологияси, ўпка шиши, ўпка, стресс омиллари, иммобилизация, гипотермия, ўпка қон айланиши, кардиореспиратор тизим, реограмма.

Relevance

A pandemic was declared by the World Health Organization on March 11, 2020. The cause of the disease was declared a new coronavirus 2 (SARS-CoV-2), which causes severe acute respiratory syndrome. [1] This epidemic disease, called COVID-19, has affected the lifestyles, economies, social lives and education of billions of people. The disease, which is highly contagious and has no fully medically proven cure, has caused more than 1.94 million deaths worldwide by January 2021. Symptoms in patients with COVID-19 vary greatly from person to person, and it can take up to 14 days for symptoms to appear. [2] Fever, fatigue, and a dry cough are the most common symptoms that can easily be mistaken for a cold or the flu. [3]

Purpose of the study: To study the literature on changes in the structure of the respiratory organs under the conditions of COVID-19.

Results and discussions

Currently, in connection with the COVID-19 pandemic, the attention of many researchers is directed to studying the dynamics of respiratory and circulatory changes in organs and tissues, as well as to studying ways to prevent this disease [1–3]. Complications of COVID-19 may include respiratory failure and sudden respiratory distress syndrome, heart failure and arrhythmias, kidney failure, multiple organ failure and death. COVID-19 is primarily known as a respiratory disease [2, 3]. Of course, the lungs and airways are the focus of COVID-19 respiratory disease. Since the new pathogen SARS-CoV-2 mainly affects the lower respiratory tract, infected individuals who experience moderate to severe illness have a dry cough, shortness of breath and/or pneumonia [3, 4].

Today, against the backdrop of a serious COVID-19 pandemic, the need for biological modeling of diseases in small laboratory animals is particularly acute. There are data in the literature on the normal values of the main indicators of blood dynamics in the systemic and pulmonary circulation, such as vascular tone, blood filling, the degree of hydration of the lung tissue, depending on the severity of venous blood stasis [6, 7].

As the experience of many years of studying stress shows, it is a standard adaptive reaction in response to the action of a large number of factors of different nature (intoxication, blood loss, trauma, infectious process, prolonged physical or mental stress, etc.), potentially threatening the existence of the organism. Regardless of the cause that caused it, the stress response is based on increased production of adrenocorticotropic hormone (ACTH) and the hyperproduction of steroid hormones induced by it by the adrenal glands. The picture of stress was first described by G. Selye in 1936 as a “syndrome caused by various harmful agents”, which later became known as a general adaptation syndrome, or biological stress syndrome [8, 9].

The literature also contains a large number of works devoted to the study of systemic and pulmonary hemodynamics in vascular diseases of the respiratory system using rheopulmonography. However, the clinical significance of rheographic data in patients with circulatory disorders in the pulmonary circulation, as well as the functional and morphological features of lung tissue, remain insufficiently studied, and the interpretation of the obtained

results in practical work presents significant difficulties.

Information about rheographic parameters in normal conditions and in violation of pulmonary blood flow is very scarce and contradictory. Thus, multidirectional changes in systemic and regional hemodynamics to the same stress in different animal species were noted by a number of researchers [2, 3, 10].

The foregoing indicates the need for a more detailed study and clarification, namely, the dynamics of rheographic parameters in normal conditions and in violation of pulmonary blood flow [10–12].

Based on the experiments conducted by K.M. Khamchiev, Z.K. Isaeva and others who conducted a study on 30 rats divided into three groups. Group 1 - intact animals (8 rats).[21]

Apart from light anesthesia and rheogram recording, these animals were not subjected to experimental influences.

group 2 - 8 rats, healthy animals, in which, after opening the chest, the histological characteristics of the lung tissue were studied.

group 3 - experimental (14 white rats), in which rheopulmonographic parameters, morphological and physiological changes in the lungs were studied in case of combined stress alteration of the lungs with a forced decrease in motor activity and a decrease in ambient temperature. The combined effect of hypothermia and immobilization was caused by the fixation of animals in a cramped chamber, the volume of which was 80 cm3, for 10 days for 6 hours. The chamber, due to small holes, had communication with the environment, where the temperature was maintained at + 3 + 4 °C [10, 12].

Where we got the following results:

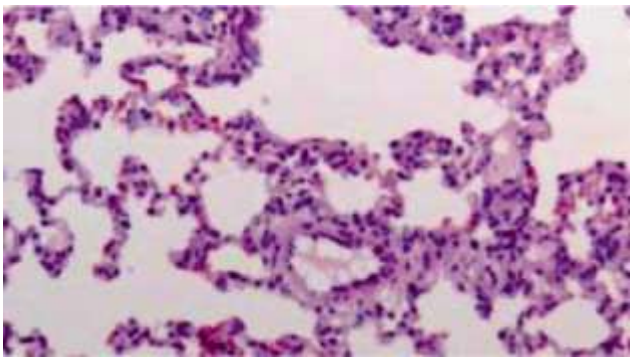
The respiratory rate in healthy animals was 76 ± 3.03 min-1. At the same time, 0.33 ± 0.01 s accounted for the inspiratory phase, and 0.32 ± 0.01 s for the expiratory phase; the respiratory pause was very short and it was not possible to measure its duration.

The rheographic curve of healthy animals resembled a conventional sphygmogram, which consisted of an ascending systolic section, reflecting blood flow to the pulmonary vessels, and a gentle diastolic segment, which, depending on the presence and height of the dicrotic wave,

indicates the nature of the venous flow of blood to the heart.

It was also found that the duration of the phases of expulsion of blood from the heart and the period of tension of its myocardium remain unchanged regardless of the phases of the respiratory cycle. However, the amplitude indicators of the rheopulmonogram differ significantly on inhalation and exhalation. In healthy animals, the systolic wave amplitude was 1.12 ± 0.04 Ω, while the diastolic amplitude was 0.68 ± 0.03 Ω. The rheographic index was equal to 0.5 Ohm. The systolic-diastolic ratio was 1.65 ± 0.09. On expiration, Ac and Ad decreased to 0.42 ± 0.07 Ω and 0.59 ± 0.08 Ω, respectively. At the same time, RI changed insignificantly and was equal to 0.47 ± 0.02 Ω, however, the systolic-diastolic ratio decreased significantly - to 0.71 ± 0.08 Ω, which indicated the difficulty of venous return of blood to the heart through the pulmonary vein system.

Histological examination of the lung tissue of healthy intact rats revealed that most of the lung parenchyma is pulmonary alveoli, which are lined with a flattened alveolar epithelium. There are thin septa between the alveoli, in which capillaries are traced without signs of erythrostasis, diapedetic hemorrhages are not found in the lumen of the postcapillary venule, and there are no signs of edema of the interalveolar septa. Lymphatic follicles in the composition of the bronchi were rarely found.



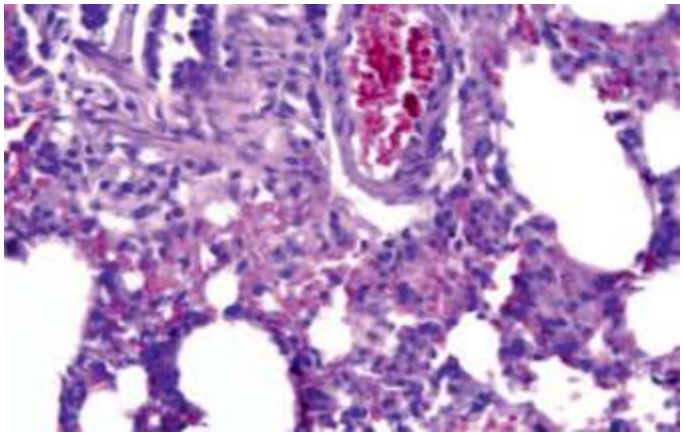
Lung tissue of a healthy rat. Coloring hematoxylin and eosin. Magnification x 200

Changes in RG during stress-induced alteration showed that on the first day, up to 1 hour of the experiment, there was a persistent trend towards a decrease in the level of blood filling of the pulmonary vessels (the weight coefficient decreased from 1.3 to 0.6). This was indicated by the change in time RG parameters [21]: shortening of time intervals reflecting periods of complete expulsion of blood from the heart and myocardial tension, decrease in AFC). Amplitude indicators also indicated an increase in vascular tone at the level of the microcirculatory bed (decrease in As, increase in blood pressure, decrease in the systolic-diastolic ratio of Ac / blood pressure below unity).

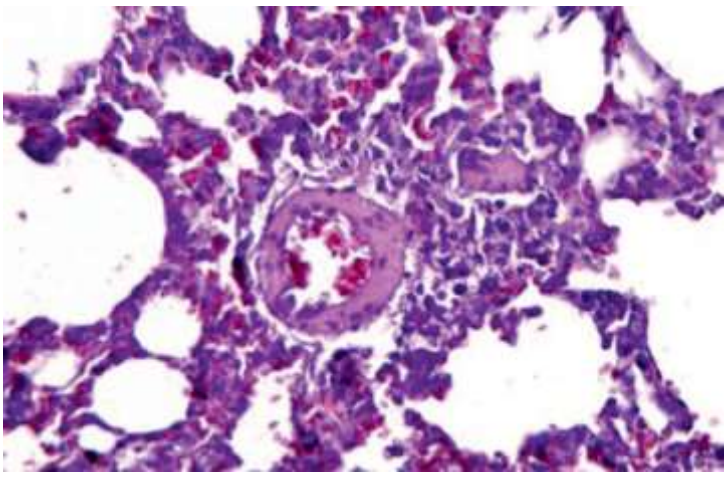
Subsequently, 1 hour after the onset of stress exposure, probably due to the adaptation of animals to extreme conditions and the inclusion of mechanisms to counteract stress, the listed changes tended to normalize (to the level of control animals). At this time, the amplitude and time parameters in all rats of the control group, with the exception of two, did not differ from those in healthy animals. However, after the second hour of the experiment, changes similar to those noted in the first hour of the experiment occurred again, and moreover, they were aggravated.

These violations persisted until the last day of the experimental series.

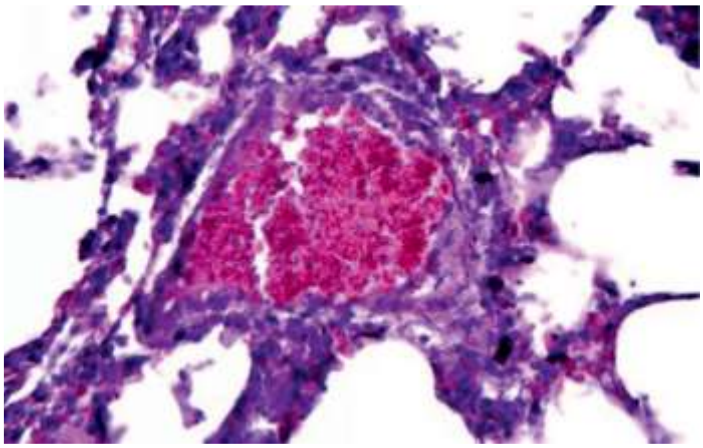
The histological picture of the lung tissue of animals of group 3a (stained with hematoxylin and eosin; magnification x200) indicated significant shifts in microcirculatory circulation, which manifested itself in sections as signs of erythrocyte stasis at the level of post-capillary capillaries, edema of the interalveolar septa. In the lung tissue of experimental rats, the development of acute plethora of capillaries and postcapillary venules with stasis of erythrocytes was noted. Edema of the interalveolar septa and diapedetic hemorrhages from capillary vessels were noted (Fig. 2).



Also distinguishing features at this time were fibrinoid swelling of the walls of arterioles, which were fragmentary spasmodic and a small amount of red blood cells was found in their lumens. There was plethora and paresis of dilated capillaries, which indicated progressive tissue hypoxia (Fig. 3).



Against the background of plethora of the venous part of the microvasculature, partial spasm and anemia of arterioles were noted, and fibrinoid swelling in the vascular walls (Fig. 4).



Paresis of capillaries. Slugging of erythrocytes

Disorder of microhemocirculation was accompanied by paretic expansion of capillaries.

On the tenth day in rats of group 3b, even more serious disorders were noted (staining with hematoxylin and eosin, x200 magnification): bronchospasm was observed with focal proliferation and desquamation of the epithelial tissue of the bronchial mucosa, dystelectasis of the lung parenchyma and the presence of erythrocytes in the lumen of the slit-like alveolar ducts, hemorrhages in peribronchial tissue with diapedesis of erythrocytes into the bronchial lumen, diapedesis of lymphocytes with lymphocytic infiltration of the bronchial wall and interalveolar septa against the background of increased blood filling and focal emphysema.

Findings

Thus, the main hemodynamic disturbances caused by the combined influence of two stress factors - prolonged immobilization and low temperature, are manifested in a decrease in the level of blood filling of the pulmonary vessels, an increase in the tone of the precapillaries and venous stasis of blood in the lungs. Histological and physiological disorders of the lung tissue indicate developing reactive bronchospasm and tissue hypoxia, the extreme manifestations of which are focal emphysema and distelectasis of the pulmonary parenchyma.

The results of the work will help theorists and doctors to better understand the mechanisms of changes occurring in organs and tissues under the influence of combined stress during the COVID-19 pandemic. It will also be useful for identifying the characteristics of cardiovascular complications, developing risk models for pulmonary and cardiac complications, as well as for theoretical substantiation of treatment methods.

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