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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

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ნამიკის შესწავლისათვის პაციენტებს სამი თვის განმავლობაში ენიშნებოდა მეტფორმინი (Acino) დღეღამური დოზით 850 მგ. დნმ-ის დაზიანების ანალიზი ხორციელდებოდა ფოსფორილირებული ჰისტონური ცილის HAX (γ-H2AX) კერების შეფასების საშუალებით სისხლის ლიმფოციტებზე (AKLIDES, Nuk Human Lymphocyte Complete, Medipan, Blankenfelde-Mahlow, გერმანია).

მეტფორმინის მიღების ფონზე შეიცვალა გაწყვეტის დიამეტრი და შეადგინა მკურნალობამდე 0,45±0,23, მკურნალობის შემდეგ - 0,44±0,27, სტატისტიკურად სარწმუნო განსხვავებანი აღმოჩენილი არ იყო. დინამიკის შეფასებისას გამოვლინდა ამ მაჩვენებლის მნიშვნელოვანი შემცირება - 2,60% ($p<0.0001$; $z=9,97$).

მკურნალობამდე გაწყვეტების საშუალო რაოდენობამ ერთ უჯრედზე შეადგინა 0,57±1,32, მეტფორმინის დანიშვნის შემდეგ შემცირდა 0,27±0,56-მდე, ცვლილებები უმნიშვნელოა. თუმცა, დინამიკის ანალიზისას მკურნალობამდე და მკურნალობის შემდეგ აღინიშნა მაჩვენებლის შემცირება 52,18%-ით ($p<0.0001$; $z=9,97$).

მეტფორმინის გამოყენება დღეღამური დოზით 850 მგ სამი თვის განმავლობაში სიმსუქნის დროს იწვევს უჯრედების გაწყვეტის დიამეტრის და γ–H2AX კერების საშუალო რაოდენობის შემცირებას, რაც მოქმედებს ონკოპათოლოგიის განვითარების რისკის შემცირებაზე. აუცილებელია შემდგომი კვლევების ჩატარება მეტფორმინის დამცველობითი მოქმედების მექანიზმის განსაზღვრისათვის არასტაბილურ გენომთან მიმართებით, განსაკუთრებით დნმ-ის დაზიანების რეაქციებთან და აპიგენეტიკურ ცვლილებებთან დაკავშირებით.

HISTOLOGICAL AND HISTOCHEMICAL FEATURES OF LIVER AND LUNG TISSUE IN PATIENTS WITH NONALCOHOLIC STEATOHEPATITIS AND OBESITY DEPENDING ON THE PRESENCE OF COMORBID CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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The comorbid course of nonalcoholic steatohepatitis (NASH) on the background of obesity and chronic obstructive pulmonary disease (COPD) has a number of clinical features and is characterized by the syndrome of mutual burden. The gold standard for the diagnosis of NASH is histopathological examination of the liver tissue samples obtained by the targeted or percutaneous liver biopsy [9,12,17].

Some studies have found a connection between fibrogenesis in the liver and lungs [1,4,11,16,20,21] and published the findings of a prospective cohort study which included 111 patients with mild and severe stages of COPD (Grenoble, France) in the European Respiratory Journal. 41.4% of patients had moderate steatosis (SteatoTest score ≥0.57), 36.9% had NASH (NashTest >0.25) and 61.3% of patients had liver fibrosis ≥F0-F1 (FibroTest ≥0.22). This indicates the prevalence of progressive forms of NAFLD among patients with COPD and may contribute to concomitant cardiometabolic diseases [21]. But there are no large-scale randomized trials of a link between decreased lung function and NASH.

It has recently been observed that adipocytes can accumulate in the lungs of obese people, thus creating an abnormal site of ectopic fat deposition and playing a role in enhancing inflammatory infiltration in the lungs [3]. The accumulation of adipose tissue can further increase the thickness of the bronchial wall and the restriction of airflow. The theory is that adipose tissue associated with the respiratory tract contributes to obstructive disease in obese individuals, as evidenced by a positive correlation with bronchial wall thickness and inflammatory activity.

Objective - to establish the pathomorphological features of liver and lung tissue in the isolated and comorbid course of NASH and COPD on the background of obesity.

Material and methods. Due to the need for a comparative study of the pathohistological structure of the liver and lung tissues, as well as preservation for the immunohistochemical (IHC) studies of the antigen integrity in the liver and lung structures there was used autopsy material of 27 cases of NASH, class I obesity with comorbid COPD stage II-III (14 cases, Group 2) and without COPD (13 cases, Group 1), namely early autopsies - up to 1 hour after the establishment of the fact of the dead's biological death from various causes (traumatic brain injury, acute stroke, sudden coronary death), in addition the deceased had NASH, obesity, COPD stage II-III during their lifetime. For comparison, we used the autopsy material of 12 patients with isolated stage II-III COPD. (Group 3), as

well as 11 practically healthy individuals (PHI), whose death was caused by polytrauma or traumatic brain injury or sudden coronary death. The groups were randomized by age, sex, and obesity class. The mean age of patients was 59.3±3.21.

Fresh material (biopsies and pieces of liver, lungs, cut with a new razor blade at autopsy) was fixed for 22 hours in a neutral buffered 10% aqueous solution of formalin according to R. Lilly [10], followed by dehydration in an ascending ethanol battery and paraffin filling. Slices of 5 μm thick were made from paraffin blocks on a sled microtome. Paraffin sections were mounted on non-immunogenic slides SuperFrost®Plus (Germany). The sections were stained with hematoxylin and eosin for review purposes. To identify the components of CT, we used the method of N.Z. Slinchenko [14] ("chromotrope 2B" – "aqueous blue" after pickling with phosphoric-tungstic acid). This method specifically stains collagen fibers blue, fibrin crimson, erythrocytes ruby red, and the connective tissue matrix looks transparent. Lipocytes (fat cells) in this histochemical technique look the same as when stained with hematoxylin-eosin, i.e. cells are round or oval in shape with very clear contours, transparent cytoplasm and a pyknotic nucleus displaced to the periphery.

When making histochemical reactions the standardization of the methods protocol for all sections was followed. The negative and positive controls were performed. When performing histological examinations there was used a biological microscope Delta Optical Evolution 300 Trino Plan LED; magnification x40, x100, x400, x600, x1000 (x10 ocular lens; x4, x10, x40, x60, x100 field lenses). Digital copies of optical images of microscopic specimens were obtained using an Olympus C740UZ camera using different microscope lenses depending on the purpose of the analysis. Micromorphomeric studies were performed using a cytology analyzer with software "VideoTest - Size 5.0" (2000) at the Department of Pathologic Anatomy of Bukovinian State Medical University.

The study was carried out in compliance with the basic provisions of the GCP (1996), the Council of Europe Convention on Human Rights and Biomedicine (dated 04.04.1997), the Helsinki Declaration of the World Medical Association on the ethical principles of scientific medical research with human participation (1964-2013), the Order of the Ministry of Health of Ukraine #690 dated 23.09.2009, #616 dated 03.08.2012.

The statistical analysis of the results was performed according to the type of study and the types of numerical data that were obtained. The normality of the distribution was checked using Lilliefors, Shapiro-Wilk tests and the method of direct visual evaluation of histograms of the distribution of eigenvalues. The quantitative values that had a normal distribution are presented as mean (M)±standard deviation (S). The discrete values are presented in the form of absolute and relative frequencies (percentage of observations to the total number of subjects). We used parametric tests to assess Student's t-test, Fisher's F-test for comparisons of data that had a normal distribution. In the case of abnormal distribution there was used: median test, calculation of the Mann-Whitney rank U-test, for multiple comparison there was used Wilcoxon rank-sum test (in the case of the study of dependent groups). For statistical and graphical analysis of the obtained results we used software packages Statistica for Windows version 8.0 (Stat Soft Inc., USA), Microsoft Excel 2007 (Microsoft, USA).

Results and discussion. When comparing the histological structure of sections of liver tissue, no differences were found in Groups 1 and 2 of comparison for all phenomena of exudation, as well as for such manifestations of proliferation as an increase in the number of binuclear hepatocytes and ductal reactions. The manifestations of alteration had the most significant differences. The morphometric parameters that characterize the average level of various manifestations of proliferation are shown in Table 1. Before characterizing the alternative liver reactions of patients in different study groups, it should be noted that in the PHI group they were not registered except for reversible swelling of hepatocytes in the form of granular dystrophy (less 1%).

Taking into account the idea of this study in case of NASH the most interesting were such phenomena of hepatocyte alteration as hepatocyte steatosis and fatty necrosis of these cells. Hepatocyte steatosis was recorded on the basis of small, medium and large droplets of fat in hepatocytes with the presence of unchanged nuclei in these cells. Fat necrosis was determined in hepatocytes on the basis of the absence of cell nuclei (karyolysis) with the presence of large droplets of fat.

Based on the data of Table 1 it is seen that in case of isolated COPD in the liver, despite the lack of clinical data on NASH, there is still a slight steatosis of hepatocytes. It covered less than 5% of hepatocytes. Hepatocyte steatosis in case of COPD can be explained by hypoxia, which develops in chronic lung pathology, which in some cells (hepatocytes, neurocytes, cardiomyocytes) leads to a characteristic violation of lipid metabolism with the development of steatosis in addition to reversible swelling and oncosis. Thus, in case of COPD in a significant percentage of hepatocytes (Table 1), in addition to steatosis, there were signs of reversible swelling of the cell in the form of granular dystrophy, in some hepatocytes there were signs of oncosis or fatty necrosis, and in single hepatocytes there was observed a deposition of golden granular pigment, which morphologically was identified as lipofuscin. As expected, many (approximately a quarter) hepatocytes in the state of steatosis were found in obese patients with NASH (Fig. 1). The percentage of hepatocytes in the state of granular dystrophy was comparable to the patients with isolated COPD, but in case of NASH on the background of obesity there were significantly more hepatocytes with signs of death (fat necrosis or oncosis) - in the amount of more than 7% (Table 1). Although the number of hepatocytes with lipofuscin in obese patients with NASH was

still small, on average less than 2%, the prevalence of this process in hepatocytes was higher ($p<0.05$) than in the patients with isolated COPD.

The patients with obesity in case of NASH and COPD had the highest percentage of hepatocytes in the state of steatosis (1.9 times compared with NASH, $p<0.05$) (Fig. 2). At the same time, in this group of study there was also noted the largest percentage of hepatocytes in a state of necrosis (1.6 times higher in comparison with an indicator in case of NASH, $p<0.05$), fatty necrosis or oncosis (2.1 times higher in comparison with an indicator in case of NASH, $p<0.05$) - together almost 13% on average. The fact of a significant increase in the percentage of hepatocytes with manifestations of lipofuscinosis (3.1 times higher in comparison with an indicator in case of NASH, $p<0.05$) (Table 1, Fig. 2) should also be noted.

Table 1. Indicators of hepatocytes, according to the morphological studies in patients with non-alcoholic steatohepatitis and obesity, depending on the presence of comorbid COPD and in practically healthy individuals (M±m)

Indicators, units of measurement	PHI, n=11	Groups of examined patients		
		NASH+obesity (Group1), n=13	NASH, obesity with COPD (Group 2), n=14	COPD (Group 3), n=12
Percentage of hepatocytes in a state of steatosis (%)	absent	24,2±0,64 *	46,4±1,12 */**	4,8±0,31 */**/***
Percentage of hepatocytes in a state of necrosis (%)	absent	5,2±0,27 *	8,5±0,34 */**	0,2±0,01 */**/***
Percentage of hepatocytes in a state of granular dystrophy (%)	0,2±0,02	38,1±1,98 *	38,6±1,94 *	39,4±2,02 *
Percentage of hepatocytes in a state of oncosis (%)	absent	2,6±0,12 *	5,4±0,17 */**	0,8±0,03 */**/***
Percentage of hepatocytes with signs of lipofuscinosis (%)	absent	1,4±0,10 *	4,3±0,22 */**	0,1±0,01 */**/***

*notes: * - the difference is probable in comparison with the indicator in PHI ($p<0,05$);*
*** - the difference is probable in comparison with the indicator in patients with NASH ($p<0,05$);*
**** - the difference is significant compared with patients with NASH with COPD ($p<0,05$)*

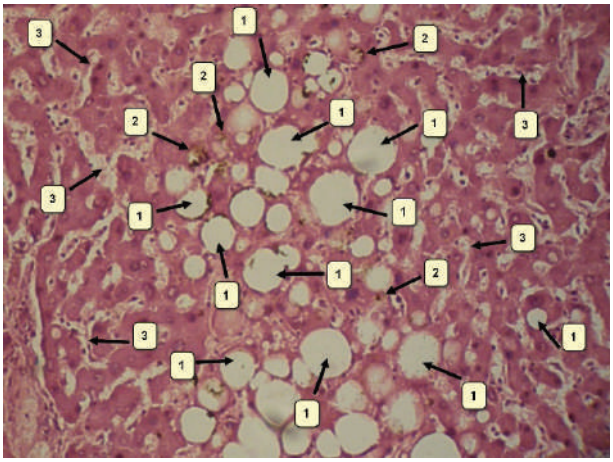

Fig. 1. Photomicrograph of the liver with obesity in case of NASH. The field of view shows hepatocytes of normal structure, which form liver beams, hepatocytes in a state of steatosis (transparent objects with clear round contours), individual hepatocytes with the pigment lipofuscin.

Figure designations: 1) Hepatocytes in a state of steatosis; 2) Pigment lipofuscin in hepatocytes; 3) Sinusoidal lumen. Staining with hematoxylin and eosin. Optical magnification 200x

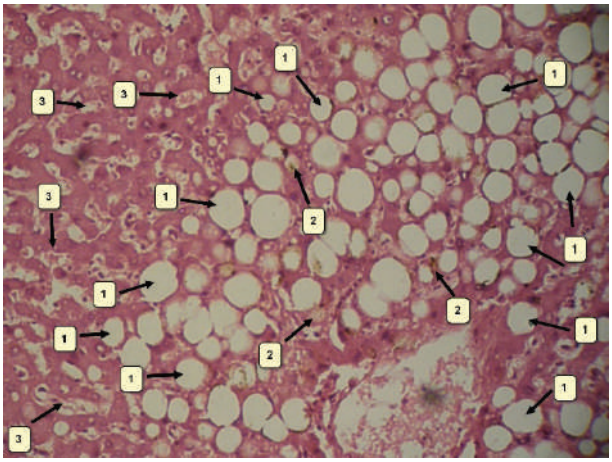

Fig. 2. Photomicrograph of the liver with obesity in case of NASH and COPD. The field of view shows hepatocytes of normal structure, which form liver beams, hepatocytes in a state of steatosis (transparent objects with clear round contours), individual hepatocytes with the pigment lipofuscin.

Figure designations: 1) Hepatocytes in a state of steatosis; 2) Pigment lipofuscin in hepatocytes; 3) Sinusoidal lumen. Staining with hematoxylin and eosin. Optical magnification 200x

Therefore, in view of the above, it can be stated that alternative phenomena in hepatocytes in obese patients with NASH and COPD were the most common and most severe among all study groups.

The microscopic examination of the peribronchial areas of some patients revealed typical lipocytes. When staining frozen sections with Sudan-III, they were stained positively in orange, therefore, they contained fats. However, lipocytes were well identified in these areas and without specific fat staining, because in preparations stained with hematoxylin and eosin or *chromotropic*-aqueous blue by N. Z. Slinchenko had all the characteristic undoubted features of these cells, including clear cytoplasm, clear contours, round shape and typical size for adipozocytes (Table 2).

Although Table 2 shows the average specific volume of lipocytes in the peribronchial CT, it should be noted that in most PHI lipocytes in the peribronchial CT were not detected at all. But in some patients they could be detected in small numbers and their diameter can be measured. It should be noted that the average lipocyte status (specific volume and size) in PHI and patients with COPD did not differ (Table 2).

Lipocytes were detected in less than half of patients with COPD. An example of a microscopic image of peribronchial tissue with individual lipocytes in a patient with COPD is shown in Figure 3. It should be noted that in case of COPD those rare lipocytes that could be found were localized in the depth of the CT, and not directly under the epithelium (Fig. 3).

A completely different picture was observed in obese patients. In particular, lipocytes in the peribronchial CT were found in all of them without exception. The only difference is that in case of NASH with obesity the volume of lipocytes in the peribronchial CT averaged more than 8% (Table 2), and in case of NASH, COPD and obesity it was even more than 14%. In addition, in the obesity cases there was a sharply increased diameter of lipocytes (Table 2).

Table 2. Indicators of lung lipocytes, according to the morphological studies in patients with nonalcoholic steatohepatitis and obesity, depending on the presence of comorbid COPD and in healthy individuals (M±m)

Indicators, units of measurement	**PHI, n=11**	**Groups of examined patients**		
		NASH+obesity (Group1), n=13	**NASH, obesity with COPD (Group 2), n=14**	**COPD (Group 3), n=12**
Specific volume of lipocytes in peribronchial connective tissue (%)	0,2±0,01	8,2±0,22 *	14,8±0,31 */**	0,5±0,02 */**/***
Average diameter of lipocytes in peribronchial connective tissue (μm)	22,4±0,38	34,2±0,46 *	39,8±0,50 */**	22,5±0,34 **/***

*notes: * - the difference is probable in comparison with the indicator in PHI (p<0.05);*
*** - the difference is probable in comparison with the indicator in patients with NASH (p<0.05);*
**** - the difference is significant compared with patients with NASH with COPD (p<0.05)*

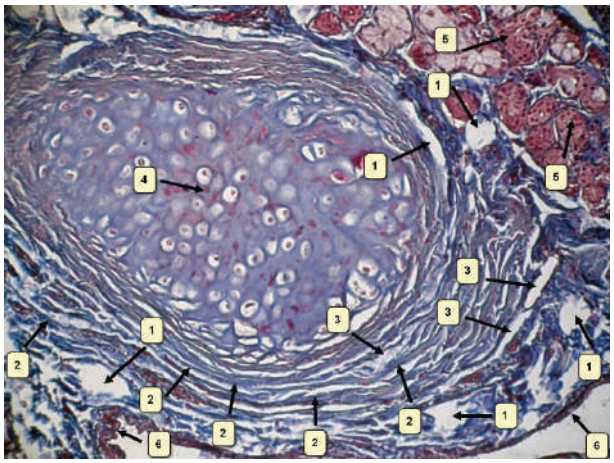

Fig. 3. Photomicrograph of the lung of a patient with COPD.

Figure designations: 1) Lipocytes; 2) Collagen fibers; 3) Connective tissue matrix; 4) Cartilage of the bronchial wall; 5) Mucous glands of the bronchus wall; 6) Bronchial surface epithelium. Staining with chromotropic-aqueous blue by N.Z.Slinchenko. Optical magnification 200

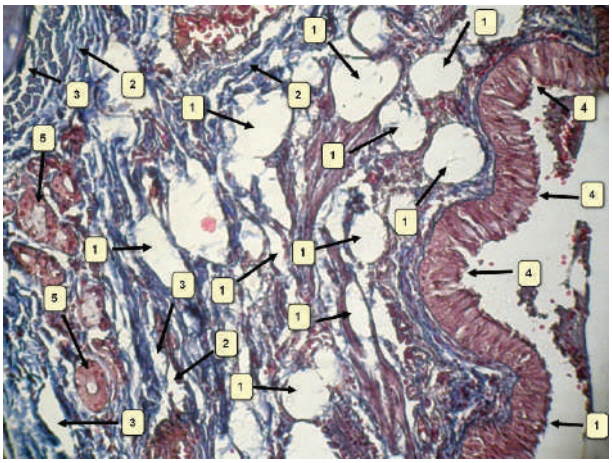

Fig. 4. Photomicrograph of the lung of an obese patient with NASH.

Figure designations: 1) Lipocytes (subepithelial location); 2) Collagen fibers; 3) Connective tissue matrix; 4) Bronchial surface epithelium; 5) Mucous glands of the bronchus wall. Staining with chromotropic-aqueous blue by N.Z. Slinchenko. Optical magnification 200x

It should also be distinguished that in the obesity cases lipocytes in the peribronchial area were located along its entire depth - from the subepithelial areas (Fig. 4,5) and to the areas in connective tissue expansion around the respiratory bronchioles and alveoli (Fig. 6,7).

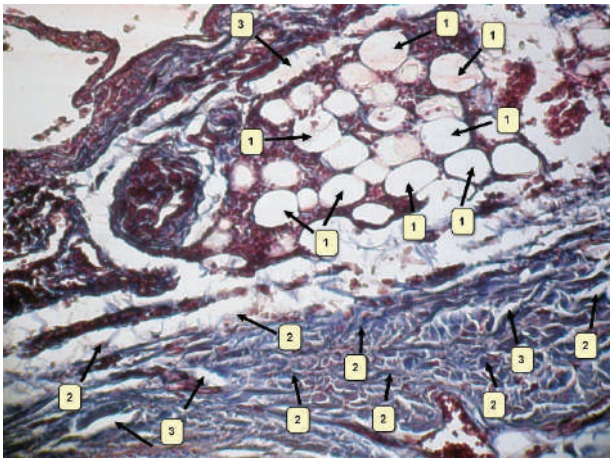

Fig. 5. Photomicrograph of the lung of a patient with NASH, COPD with obesity.

Figure designations: 1) Lipocytes (subepithelial location); 2) Collagen fibers; 3) Connective tissue matrix; Staining with chromotropic-aqueous blue by N.Z.Slinchenko. Optical magnification 200x

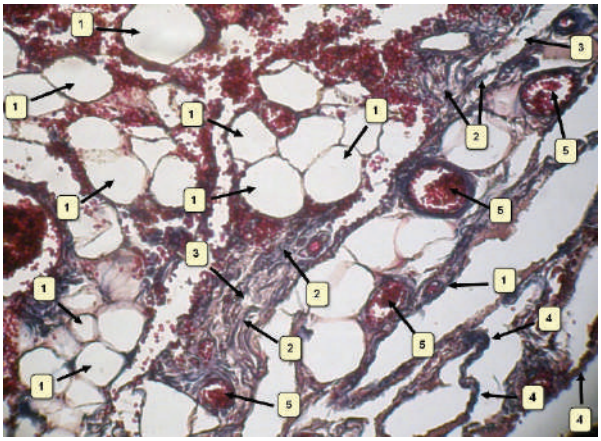

Fig. 6. Photomicrograph of the lung of an obese patient with NASH. Lipocytes are located in the expansion of connective tissue around the respiratory bronchioles and alveoli.

Figure designations: 1) Lipocytes; 2) Collagen fibers; 3) Connective tissue matrix; 4)Alveoli and respiratory bronchioles walls; 5) Blood vessels. Staining with chromotropic-aqueous blue by N.Z.Slinchenko. Optical magnification 200x

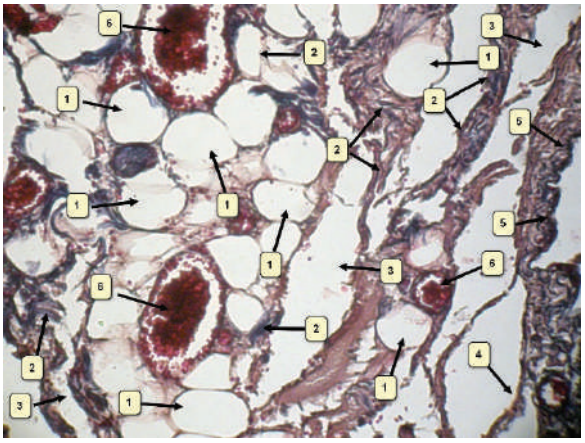

Fig. 7. Photomicrograph of the lung of a patient with NASH, COPD with obesity.
Lipocytes are located in the expansion of connective tissue around the respiratory bronchioles and alveoli.
Figure designations: 1) Lipocytes; 2) Collagen fibers; 3) Connective tissue matrix; 4) Alveoli walls; 5) Bronchioles walls; 6) Blood vessels. Staining with chromotropic-aqueous blue by N.Z.Slinchenko. Optical magnification 200x

The findings of the recent research, summarized in the reviews of Ch. Trautwein et al., A. Takaki et al., F. Stickel et al. [15,18,19], confirm the data obtained by us: the internal accumulation of excess neutral fat in hepatocytes, oxidative stress, activation of lipid peroxidation (LPO), due to reduced antioxidant defense system, lead to mitochondrial dysfunction, endocrine stress, endoplasmic reticulum stress, necrotic changes in hepatocytes [5-8]. Active oxygen species, LOPs and proinflammatory cytokines secreted by lymphocytes, Kupffer cells, and monocyte macrophages stimulate the transformation of Ito stellate cells and portal fibroblasts into myofibroblasts that are able to activate fibrogenesis processes [13].

Hepatocellular steatosis in more than 5% of hepatocytes is a hallmark of NAFLD. Macrovesicular steatosis, which begins in zone 3, is most common, but panacinar steatosis can also be observed [17]. The increase in the severity of steatosis correlates with lobular inflammation, zone 3 fibrosis and NASH [2]. Our data confirm this position, however, in the group with comorbid COPD hepatocyte steatosis was 1.9 times more intense compared with the NASH group ($p<0.05$). In case of isolated COPD, there was also a slight hepatocyte steatosis (less than 5%), which can be explained by hypoxia, which develops in chronic lung pathology, in some cells (hepatocytes, neurocytes, cardiomyocytes), which in addition to reversible

swelling and oncosis leads to lipid metabolism with the development of steatosis.

Elliot J.G. and co-authors were the first to quantify airway lipid accumulation in patients with broncho-obstructive syndrome [3]. They found a positive correlation between visceral adipose tissue area, BMI with bronchial tree wall thickness and inflammation. Thus, the accumulation of lipids in the lungs in obese patients contributes to the remodeling of the bronchi and the emergence of airflow restrictions [3,21]. There may be common pathogenetic mechanisms between circulating lipid compounds and structural components of the lungs, and bronchial remodeling is also affected by intracellular accumulation of emulsified or oxidized lipid metabolites. Given the peribronchial lipocytes found by us, which were most intensely detected in the autopsy samples of Group 2 patients ($p<0.05$), we can hypothesize the role of lipid metabolism disorders and the presence of common pathogenetic links in this type of comorbidity.

Conclusions.

1. The comorbid course of NASH, obesity and COPD revealed the maximum percentage of hepatocytes in the state of steatosis (1.9 times higher than in case of NASH with obesity, $p<0.05$), the maximum proportion of hepatocytes in the state of fatty necrosis (1.6 times more than in case of NASH, $p<0.05$), oncosis (2.1 times, $p<0.05$), and lipofuscinosis (3.1 times more than in case of NASH with obesity, p<0, 05), which indicates more significant dysmetabolic disorders and the activity of the inflammatory process in hepatocytes.

2. The combined course of obesity, NASH and COPD contributed to a significant increase in the number of lipocytes in the lungs (29.6 times, $p<0.05$) compared with isolated COPD, as well as a probable increase in their diameter (1.8 times, $p<0.05$).

Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article“**.**

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of the World Medical Association on the ethical principles of scientific medical research with human participation (1964-2013), as well as the national law. Informed consent was obtained from all the patients included in the study“.

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SUMMARY

HISTOLOGICAL AND HISTOCHEMICAL FEATURES OF LIVER AND LUNG TISSUE IN PATIENTS WITH NONALCOHOLIC STEATOHEPATITIS AND OBESITY DEPENDING ON THE PRESENCE OF COMORBID CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Objective - to establish the pathomorphological features of liver and lung tissue of patients with non-alcoholic steatohepatitis (NASH) and obesity depending on comorbidity with chronic obstructive pulmonary disease (COPD).

The study used autopsy material of 13 cases of NASH and class I obesity (Group 1), 14 cases of NASH, class I obesity with comorbid COPD of stage II-III (Group 2). For comparison, we used the autopsy material of 12 patients with isolated COPD of stage II-III (Group 3), as well as 11 practically healthy individuals (PHI), whose death was caused by polytrauma or traumatic brain injury or sudden coronary death. The groups were randomized by age, sex, and class of obesity. The average age of patients was 59.3±3.21.

In Group 2 there was a maximum percentage of hepatocytes in the state of steatosis (1.9 times more than in Group 1, $p<0.05$), 1.6 times more hepatocytes in the state of fatty necrosis compared with NASH, $p<0.05$), oncosis (2.1 times, $p<0.05$), as well as lipofuscinosis (3.1 times more than in case of NASH with obesity, $p<0.05$). The combined course of obesity, NASH and COPD contributed to a significant increase in the number of lipocytes in the lungs (29.6 times, $p<0.05$) compared with isolated COPD, as well as a probable increase in their diameter (1.8 times, $p<0.05$).

In the comorbid course of NASH, obesity and COPD, more intense histological and histochemical changes were observed, indicating more significant dysmetabolic disorders and the role of COPD in the activity of the inflammatory process in the liver, namely a higher % of steatosis in hepatocytes. Accumulation of adipocytes was observed in the lungs in this combined pathology, which probably indicates the aggravating effect of NASH and obesity on the course of COPD.

Keywords: non-alcoholic steatohepatitis, obesity, chronic obstructive pulmonary disease.

РЕЗЮМЕ

ГИСТОЛОГИЧЕСКИЕ И ГИСТОХИМИЧЕСКИЕ ОСОБЕННОСТИ ТКАНИ ПЕЧЕНИ И ЛЕГКИХ БОЛЬНЫХ НЕАЛКОГОЛЬНЫМ СТЕАТОГЕПАТИТОМ И ОЖИРЕНИЕМ В ЗАВИСИМОСТИ ОТ НАЛИЧИЯ КОМОРБИДНОЙ ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ

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Цель исследования - определить патоморфологические особенности ткани печени и легких пациентов с неалкогольным стеатогепатитом и ожирением в зависимости от коморбидности с хронической обструктивной болезнью легких.

В исследовании использован аутопсийный материал 13 случаев неалкогольного стеатогепатита (НАСГ) и ожирения I степени (группа 1), 14 случаев НАСГ, ожирения I степени с коморбидной хронической обструктивной болезнью легких (ХОБЛ) II-III стадии (группа 2). Для сравнения использовали аутопсийный материал 12 пациентов с изолированной ХОБЛ II-III стадии (группа 3), а также 11 практически здоровых

лиц, смерть которых наступила в результате политравмы или черепно-мозговой травмы, или внезапной коронарной смерти. Группы рандомизированы по возрасту, полу и степени ожирения. Средний возраст пациентов составил 59,3±3,21 г.

В группе 2 выявлен максимальный процент гепатоцитов в состоянии стеатоза (в 1,9 раза больше, чем в группе 1, p<0,05), в 1,6 раза больше гепатоцитов в состоянии жирового некроза в сравнении с НАСГ (p<0,05), онкоза в 2,1 раза (p<0,05), а также липофусциноза в 3,1 раза больше, чем при НАСГ с ожирением (p<0,05). Комбинированное течение ожирения, НАСГ и ХОБЛ способствовало достоверному увеличению количества липоцитов в легких (29,6 раза, p<0,05) в сравнении с изолированной ХОБЛ, а также вероятному увеличению их диаметра (1,8 раза, p<0,05).

При коморбидном течении НАСГ, ожирения и ХОБЛ наблюдались более интенсивные гистологические и гистохимические изменения, указывающие на значительные дисметаболические нарушения и роль ХОБЛ в активности воспалительного процесса в печени, а именно на более высокий процент стеатоза в гепатоцитах. При этой комбинированной патологии в легких наблюдалось накопление адипоцитов, что, по всей вероятности, свидетельствует об отягчающем влиянии НАСГ и ожирения на течение ХОБЛ.

რეზიუმე

არაალკოჰოლური სტეატოჰეპატიტის და სიმსუქნის მქონე პაციენტების ღვიძლის და ფილტვების ქსოვილის ჰისტოლოგიური და ჰისტოქიმიური თავისებურებები ფილტვების ქრონიკული ობსტრუქციული დაავადების კომორბიდობაზე დამოკიდებულებით

[1]ო.გრინიუკი,[1]ო.ხუხლინა,[2]ი.დავიდენკო,[1]ო.ვოევიდკა, [1]ო.მანდრიკი

ბუკოვინის სახელმწიფო სამედიცინო უნივერსიტეტი, [1]შინაგანი დაავადებების, კლინიკური ფარმაკოლოგიისა და პროფესიული დაავადებების კათედრა; [2]პათოლოგიური ანატომიის კათედრა, ჩერნოვცი, უკრაინა

კვლევის მიზანს წარმოადგენდა არაალკოჰოლური სტეატოჰეპატიტის და სიმსუქნის მქონე პაციენტების ღვიძლის და ფილტვების ქსოვილის პათომორფოლოგიური თავისებურებების განსაზღვრა ფილტვების ქრონიკული ობსტრუქციული დაავადების (ფქოდ) კომორბიდობაზე დამოკიდებულებით.

კვლევაში გამოყენებულია არაალკოჰოლური სტეატოჰეპატიტის და I ხარისხის სიმსუქნის 13 შემთხვევის (ჯგუფი 1), არაალკოჰოლური სტეატოჰეპატიტის, I ხარისხის სიმსუქნის და II-III ხარისხის ფქოდ-ის კომორბიდობის 14 შემთხვევის აუტოფსიური მასალა (ჯგუფი 2). შედარებისათვის გამოყენებული იყო აუტოფსიური მასალა იზოლირებული II-III ხარისხის ფქოდ-ის მქონე 12 პაციენტისა (ჯგუფი 3) და 11 პრაქტიკულად ჯანმრთელი პირისა, რომელთა სიკვდილი დადგა პოლიტრავმის, ქალა-ტვინის ტრავმის ან უეცარი კორონარული სიკვდილის შედეგად. ჯგუფები რანდომიზებული იყო ასაკის, სქესის და სიმსუქნის ხარისხის მიხედვით. პაციენტების საშუალო ასაკი შეადგენდა 59,3±3,21 წელს.

ჯგუფი 2-ში გამოვლინდა ჰეპატოციტების მაქსიმალური რაოდენობა სტეატოზის მდგომარეობაში - 1,9-ჯერ მეტი, ვიდრე ჯგუფი 1-ში, p<0,05), ცხიმოვანი ნეკროზის მდგომარეობაში, 1,6-ჯერ მეტი ჰეპატოციტი, ვიდრე არაალკოჰოლური სტეატოჰეპატიტის დროს (p<0,05), ონკოზის (2,1-ჯერ, p<0,05), ასევე, ლიპოფუსცინოზის (3,1-ჯერ მეტი, ვიდრე არაალკოჰოლური სტეატოჰეპატიტის და სიმსუქნის შემთხვევაში, p<0,05). სიმსუქნის, არაალკოჰოლური სტეატოჰეპატიტის და ფქოდ-ის კომბინირებული მკურნალობა ხელს უწყობდა ფილტვებში ლიპოციტების რაოდენობის სარწმუნო ზრდას (29,6-ჯერ, p<0,05), იზოლირებულ ფქოდ-თან შედარებით, ასევე, მათი დიამეტრის ზრდას (1,8-ჯერ, p<0,05).

არაალკოჰოლური სტეატოჰეპატიტის, სიმსუქნის და ფქოდ-ის კომორბიდული მიმდინარეობისას აღინიშნება უფრო ინტენსიური ჰისტოლოგიური და ჰისტოქიმიური ცვლილებები, რომლებიც მიუთითებს მნიშვნელოვანი დისმეტაბოლური დარღვევების და ფქოდ-ის როლის შესახებ ღვიძლში ანთებითი პროცესების აქტივობაზე, კერძოდ, სტეატოზის უფრო მაღალ პროცენტზე ჰეპატოციტებში. ამ კომბინირებული პათოლოგიის დროს ფილტვებში აღინიშნებოდა ადიპოციტების დაგროვება, რაც, როგორც ჩანს, მიუთითებს არაალკოჰოლური სტეატოჰეპატიტის და სიმსუქნის დამამძიმებელ მოქმედებაზე ფქოდ-ის მიმდინარეობაზე.