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CLINICAL COURSE FEATURES OF NON-ALCOHOLIC STEATOHEPATITIS ON OBESITY BACKGROUND IN COMORBIDITY WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Objective: *to elucidate clinical, ultrasonographic, and biochemical features of the course of non-alcoholic steatohepatitis (NASH) for comorbidity with grade 1 obesity, chronic obstructive pulmonary disease (COPD) of 2–3 D stages compared with NASH during obesity without COPD by studying the frequency and intensity of leading clinical and biochemical syndromes of NASH, comparison of ultrasonographic (USG) characteristics of NASH depending on the presence of COPD.*

Material and methods. *105 NASH patients were examined: 52 NASH patients with grade 1 obesity (1 group) (there were 18 men, 24 women); 53 NASH patients with comorbid grade 1 obesity and COPD of 2–3 D stages (group 2) (there were 28 men, 13 women). In order to determine the dependence of NASH on the presence of COPD, groups of patients were randomized by the age and the degree of obesity. The average age of the patients was (55,7 ± 3,22) years. The functional condition of the liver was determined by the generally accepted lists of enzyme activity, markers of pigment and nitrogen metabolism, proteinograms, lipidograms, ionograms, calculation of de Ritis ratio, and the USG was performed. In order to quantify the changes in liver echogenicity we have used the method of echodensitometry with the calculation of the hepatorenal index.*

Results. *The symptoms of astheno-vegetative syndrome, dyspepsia and feeling of heaviness or pain while palpating in the right hypochondrium were observed in 2,1 times, 1,7 times and 2,5 times ($p<0,05$) more often in patients of the 2nd group in comparison with patients of the 1st group. Clinically, in NASH patients the syndrome of cholestasis was found in 28.8%, in comparison with NASH patients and COPD (in 62,3%). In patients of the 2nd group, the frequency of splenomegaly exceeded the indicator in the 1st group, respectively, in 2.7 times ($p<0.05$). Among the biochemical syndromes in the examined patients of the 2nd group was found cytolytic (100,0%), cholestatic (73,6%) syndromes, which exceeded the frequency in the 1st group in 2,3 times ($p<0,05$), mesenchymal inflammatory, which occurred more often as compared to the 1st group — in 1.9 times ($p<0,05$), and hepatocellular failure (HF) syndrome (50,9%), which occurred more often in comparison with the 1st group — in 2,6 times ($p<0,05$).*

Conclusion. *The clinical course of non-alcoholic steatohepatitis for comorbidity with obesity is characterized by a high frequency and intensity of clinical syndromes, the manifestation of which increases significantly with the addition of COPD 2–3 D namely: astheno-vegetative, abdominal pain, portal hypertension, splenomegaly, cholestasis, as well as the frequency and intensity of biochemical syndromes namely: mesenchymal inflammation, cholestasis, hepatocellular failure.*

Ключевые слова: *неалкогольный стеатогепатит, ожирение, хроническая обструктивная болезнь легких, клинические*

ОСОБЕННОСТИ КЛИНИЧЕСКОГО ТЕЧЕНИЯ НЕАЛКОГОЛЬНОГО СТЕАТОГЕПАТИТА НА ФОНЕ ОЖИРЕНИЯ ПРИ КОМОРБИДНОСТИ С ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНЬЮ ЛЕГКИХ

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синдромы, стеатоз печени.

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Цель работы *— выяснить клинические, ультрасонографические и биохимические особенности течения неалкогольного стеатогепатита (НАСГ) при коморбидности с ожирением I степени, хронической обструктивной болезнью легких (ХОБЛ) 2–3-ей стадий D по сравнению с течением НАСГ на фоне ожирения без ХОБЛ путем изучения частоты и интенсивности ведущих клинических и биохимических синдромов НАСГ, сравнение ультрасонографических (УСГ) характеристик НАСГ в зависимости от наличия ХОБЛ.*

Материал и методы. *Обследовано 105 больных НАСГ из которых 52 больных НАСГ с ожирением I ст. (1-ая группа) (мужчин было 18, женщин — 24), 53 больных НАСГ с ожирением I ст. и ХОБЛ 2–3 D (мужчин было 28, женщин — 13) (2-ая группа). Для определения зависимости течения НАСГ от наличия ХОБЛ группы больных были рандомизированы по возрасту и степени ожирения. Средний возраст пациентов составил (55,7 ± 3,22) лет. Определяли функциональное состояние печени по общепринятым перечнем активности ферментов, маркеров пигментного и азотистого обмена, протеинограммы, липидограммы, ионограммы, вычисления коэффициента де Ритиса, проводили УСГ исследования. С целью количественной оценки изменений эхогенности печени использовали метод еходенситометрии с вычислением гепаторенального индекса (ГРИ).*

Результаты. *У больных 2-ой группы симптомы астено-вегетативного синдрома, диспепсии, ощущение тяжести или болезненность при пальпации в правой подреберной области наблюдались чаще в 2,1 раза, 1,7 раза и в 2,5 раза*

(p <0,05) в сравнении с больными 1-ой группы. Клинически синдром холестаза был установлен в 28,8% больных НАСГ и у 62,3% с НАСГ и ХОБЛ. У больных 2-ой группы частота спленомегалии превысила показатель в 1-й группе соответственно в 2,7 раза (p <0,05). Среди биохимических синдромов у обследованных больных 2-ой группы было установлено цитолитический (100,0%), холестатический (73,6%), который превышал по частоте показатель в 1 группе в 2,3 раза (p <0,05), мезенхимально-воспалительный, который возникал чаще чем в 1-ой группе — в 1,9 раза (p <0,05), и синдром печеночноклеточной недостаточности (ПКН) (50,9%), который случался чаще чем в 1-ой группе — в 2,6 раза (p <0,05).

Вывод. *Клиническое течение неалкогольного стеатогепатита при коморбидности с ожирением характеризуется высокой частотой и интенсивностью клинических синдромов, манифестация которых достоверно возрастает в условиях присоединения ХОБЛ 2–3 D: астено-вегетативного, абдоминально-болевого портальной гипертензии, спленомагалии, холестаза а также частотой и интенсивностью биохимических синдромов: мезенхимального воспаления, холестаза, ПКН.*

Ключові слова: *неалкогольний стеатогепатит, ожиріння, хронічне обструктивне захворювання легень, клінічні синдроми, стеатоз печінки.*

ОСОБЛИВОСТІ КЛІНІЧНОГО ПЕРЕБІГУ НЕАЛКОГОЛЬНОГО СТЕАТОГЕПАТИТУ НА ТЛІ ОЖИРІННЯ ЗА КОМОРБІДНОСТІ З ХРОНІЧНИМ ОБСТРУКТИВНИМ ЗАХВОРЮВАННЯМ ЛЕГЕНЬ

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Мета роботи *— з'ясувати клінічні, ультрасонографічні та біохімічні особливості перебігу неалкогольного стеатогепатиту (НАСГ) за коморбідності з ожирінням I ступеня, хронічним обструктивним захворюванням легень (ХОЗЛ) 2–3-ї стадій D порівняно з перебігом НАСГ на тлі ожиріння*

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без ХОЗЛ шляхом вивчення частоти та інтенсивності провідних клінічних та біохімічних синдромів НАСГ, порівняння ультрасонографічної (УСГ) характеристики НАСГ залежно від наявності ХОЗЛ.

Матеріал і методи. *Обстежено 105 хворих на НАСГ з яких 52 хворих на НАСГ із ожирінням I ст. (1-ша група) (чоловіків було 18, жінок — 24 особи), 53 хворих на НАСГ із ожирінням I ст. та ХОЗЛ 2–3 D (чоловіків було 28, жінок 13 осіб) (2-га група). Для визначення залежності перебігу НАСГ від наявності ХОЗЛ групи хворих рандомізовані за віком, ступенем ожиріння. Середній вік пацієнтів склав (55,7±3,22) років. Визначали функціональний стан печінки за загальноприйнятим переліком активності ферментів, маркерів пігментного та азотистого обміну, протеїнограми, ліпідограми, іонограми, обчислення коефіцієнта де Рітіса, проводили УСГ дослідження. З метою кількісної оцінки змін ехогенності печінки використали метод еходенситометрії з обчисленням гепаторенального індексу (ГРІ).*

Результати. *У пацієнтів 2-ї групи симптоми астено-вегетативного синдрому, диспепсії, відчуття тяжкості або болючість при пальпації у правій підреберній ділянці спостерігалися частіше у 2,1 раза, 1,7 раза та у 2,5 раза ($p<0,05$) порівняно з хворими 1-ї групи. Клінічно синдром холестазу встановлено у 28,8% хворих на НАСГ та у 62,3% хворих на НАСГ та ХОЗЛ. У пацієнтів 2-ї групи частота спленомегалії перевищила показник у 1-й групі відповідно у 2,7 раза ($p<0,05$). Серед біохімічних синдромів у обстежених осіб 2-ї групи встановлено цитолітичний (100,0%), холестатичний (73,6%), який перевищував за частотою показник у 1-й групі у 2,3 раза ($p<0,05$), мезенхімально-запальний, який виникав із вищою частотою, ніж у 1-й групі — в 1,9 раза ($p<0,05$), та синдром печінковоклітинної недостатності (ПКН) (50,9%), який виникав з вищою частотою, ніж у 1-й групі — у 2,6 раза ($p<0,05$).*

Висновок. *Клінічний перебіг неалкогольного стеатогепатиту за коморбідності з ожирінням характеризується вищою частотою та інтенсивністю клінічних синдромів, маніфестація яких вірогідно зростає за умов приєднання, хронічного обструктивного захворюванням легень 2–3 D: астено-вегетативного, абдомінально-больового, портальної гіпертензії, спленомагалії, холестазу; а також частота та інтенсивність біохімічних синдромів: мезенхімального запалення, холестазу, печінковоклітинної недостатності.*

Introduction. The relevance of the problem of the combined course of non-alcoholic steatohepatitis (NASH) on the background of obesity with chronic obstructive pulmonary disease (COPD) is a significant increase in the frequency of this type of disease (24–30%) [1, 2]. NASH is detected in 38.5–56%, liver cirrhosis in 9–10% of cases at autopsy among patients with type 2 diabetes mellitus (DM) and obesity [3–5]. The impetus for the NASH development are metabolic disorders due to obesity, insulin resistance syndrome (IR), lipid distress syndrome, activation of oxidative (OS) and nitrosative stress (NS), impaired oxidative antioxidant homeostasis, hepatocyte steatosis, aseptic inflammation, induction of apoptosis and necrosis of hepatocytes activating fibroblasts system with progression of liver fibrosis [6–14].

A number of these factors are also inherent in the pathogenesis of COPD, in particular, OS, NS, antioxidant deficiency, local and systemic inflammation, activation of fibroblasts with progression of bronchial remodeling and pneumosclerosis [1, 2]. At the same time, β2 agonists, anticholinergics inhaled or systemic glucocorticoids, repeated courses of antibacterial drugs, which together can influence the development of dysmetabolic disorders and even hepatotoxic effects, are used in the treatment of COPD patients [2]. At the same time, the course of COPD stage 3–4 in patients of group D with a duration of more than 15 years is often complicated by the development of a chronic pulmonary heart disease, against which hepatomegaly, edematous-ascitic syndrome can be formed. Now the clinical features of the course of comorbidity of NASH and COPD are little studied, which necessitates the investigation of general developmental mechanisms, reciprocal mechanisms and the development of new methods for the correction of this comorbid pathology.

Aim of work: To find out clinical, ultrasonographic and biochemical features of NASH course of obesity of the I grade, COPD of the 2–3 stages D comorbidities in comparison with the course of NASH with obesity without COPD by studying the frequency and intensity of leading clinical and biochemical syndromes, ultrasonographic (USG) characteristics of NASH depending on the presence of COPD.

Material and research methods. 105 NASH patients were examined: 52 among them of were NASH patients with grade I obesity (group 1) (men were 18, women were 24 people), 53 NASH patients with grade I obesity and COPD of the 2–3 stages D (28 males, 13 females) (group 2). To determine the dependence of NASH on COPD, groups of patients were randomized by age, degree of obesity. The average age of the patients was (55.7 ± 3.22) years.

The diagnosis of NASH was established according to the unified clinical protocol approved by the order of the Ministry of Health of Ukraine No. 826 of November 6, 2014, in the presence of criteria for the exclusion of chronic diffuse liver disease, of viral, hereditary, autoimmune or drug genesis as a cause of cytolytic, cholestatic syndromes, as well as USG results examination with shear wave elastography, SteatoTest (Sinevo). The diagnosis and treatment of COPD was carried out according to the recommendations of clinical guidelines (Order of the Ministry of Health of Ukraine No. 555 of 06/27/2013, taking into account the recommendations of GOLD, 2019).

When patients were admitted to the hospital, the functional state of the liver was determined according to the generally accepted list of activity of enzymes, markers of pigment and nitrogen metabolism, proteinogram, lipidogram, ionogram, calculation of the De Ritis ratio. USG studies were performed to determine structural changes in the liver parenchyma. In order to quantify changes in liver echogenicity, the method of echodensitometry with the calculation of hepato-renal index (HRI) was used (Webb M. et al., 2009) [3, 4, 15]. Liver echodensitometry was performed on an empty stomach on an Ultima PA apparatus (Radmir, Kharkov, Ukraine) using a convex sensor (frequency 3–5 MHz) with subsequent digital histographic processing of USG images. HRI was calculated by the formula (Webb M. et al., 2009): HRI = MNA/MNB [15]. All patients were performed anthropometry with determination of body mass index (BMI), waist circumference (WC), hip circumference (HC) and their ratio: waist/hip index (IWH=WC/HC).

Statistical analysis of the results was carried out in accordance with the type of study and the types of numerical data that were obtained. The normality of the distribution was checked using the tests of Liliefors, Shapiro-Willkie and the method of direct visual assessment of histograms of the distribution of eigenvalues. Quantitative indicators that had a normal distribution, presented as mean (M) ± standard deviation (S). For nonparametric distribution, the data are presented as the median (Me) as a measure of position, upper (Q75) and lower quartile (Q25) as a scattering measure. Discrete values are presented in the

Table 1

Frequency of clinical and biochemical syndromes of non-alcoholic steatohepatitis depending on the presence of comorbid COPD, %

Syndromes	Groups of patients examined					
	NASH, n=52		NASH+COPD, n=53		OR	
	Abs.	%	Abs.	%	OR	Confidence Interval (CI) 95%
Asteno-vegetative	22	42,3	46	86,8	2,05	1,09-3,88
Dyspepsia	21	40,4	37	69,8	1,73	0,89-3,34
Cholestasis clinically	15	28,8	33	62,3	2,16	1,05-4,44
Discomfort in the right hypochondrium	11	21,2	28	52,8	2,59	1,17-5,71
Hepatomegaly	49	94,2	53	100,0	1,06	0,62-1,83
Splenomegaly	7	13,5	19	35,8	2,66	1,03-6,87
Cytolysis	52	100,0	53	100,0	1,0	0,58-1,72
Cholestasis, biochemically	17	32,7	39	73,6	2,25	1,13-4,47
Mesenchymal-inflammatory	25	48,1	48	90,6	1,88	1,02-3,49
Hepatocellular failure (HCF)	10	19,2	27	50,9	2,65	1,17-6,02
Impaired glucose tolerance (IGT)	23	44,2	49	92,5	2,09	1,19-3,91

Table 2

Indicators of biochemical blood test in patients with non-alcoholic steatohepatitis depending on the presence of comorbid COPD, (M±m)

Indicators, units measuring	*AHH*, n=30	Groups of patients examined	
		NASH, n=52	NASH+COPD, n=53
Bilirubin total, μmol/l	19,21±1,09	27,9±1,21 *	36,2±1,03 */**
Bilirubin direct, μmol/l	4,51± 0,22	8,3±0,23 *	10,4±0,25 */**
Bilirubin indirect, μmol/l	14,70±0,31	19,6±0,75 *	25,8±0,93 */**
AST, μmol/hour×l	0,39± 0,01	0,93±0,012 *	1,28±0,025 */**
ALT, μmol/hour×l	0,38± 0,01	1,17±0,012 *	1,44±0,011 */**
de Ritis factor	1,03± 0,02	0,79±0,005 *	0,89±0,004 */**
γ-GT, mmol/hour×l	5,20± 0,13	6,08±0,10*	6,79±0,09*/**
ALP, mmol/hour×l	1,25± 0,04	1,45±0,01 *	1,76±0,02 */**
Thymol test	2,80± 0,12	3,72±0,11 *	4,48±0,10 */**
Total protein, g/l	76,18±2,15	69,25±1,93	60,11±1,32*/**
Albumin,%	59,37±2,21	53,21±2,38	41,63±2,25 */**
Globulins,%	40,63±2,50	46,79±2,14	58,37±2,14*/**
A/G coefficient	1,46±0,002	1,14±0,004 *	0,71±0,003 */**

Notes: 1. * - the difference is probable in comparison with the indicator in *AHH* (p<0,05); 2. ** - the difference is probable in comparison with the indicator in NASH patients (p<0,05).

form of absolute and relative frequencies (percentage of observations to the total number of examined). Parametric tests with an assessment of Student's t-test, Fisher's F-test we used for comparisons of the data, which should have a normal distribution. The median test, the calculation of the rank U-test of Mann-Whitney, for multiple comparisons — the Wilcoxon T-test (in the case of the study of dependent groups) we used in the case of an abnormal distribution.

Pearson correlation analysis for parametric distribution and Spearman's rank correlation coefficient in the case of the distribution of indicators were used to estimate the degree of dependence between variables and that was significantly different from normal. To compare the discrete values in the independent groups, the log-likelihood criterion $\chi 2$ (MP $\chi 2$) was used, and the Fisher exact mid-p modification was used to compare the pairs of discrete quantities. Determination of the diagnostic superiority of the method was performed on the basis of the evaluation of the quality of diagnostic procedures using receiver operating characteristic (ROC analysis), with the calculation of indicators of sensitivity, specificity, diagnostic value, area under the ROC curve (AUROC), diagnostic odds ratio (DOR). Statistica for Windows software version 8.0 (Stat Soft inc., USA), Microsoft Excel 2007 (Microsoft, USA) we used for statistical and graphical analysis of the obtained results.

The results of the study. Clinically, in the examined patients, NASH was manifested by the following syndromes: astheno-vegetative (42.3%), dyspeptic (nausea, abdominal distension, stool disorders) (40.4%), severity or discomfort in the right hypochondrium (21.2%), hepatomegaly (94.2%), splenomegaly (13.5%), cholestatic (bitterness in the mouth, itchy skin, xanthomas, xanthelasmas on the eyelids) (28.8%) and endocrine disorders: I degree obesity was present in 100,0% patients, in 44.2%, impaired glucose tolerance (IGT) was found (Table 1). Among the biochemical syndromes in patients of the 1st group, cytolytic (100.0%), cholestatic (32.7%), mesenchymal-inflammatory syndrome (48.1%), and hepatocellular failure syndrome (HCF) (19.2%) were found.

It should be noted that in the analysis of clinical manifestations of NASH in patients of the 2nd group the frequency and intensity were significantly higher. In particular, the symptoms of astheno-vegetative syndrome were observed 2.1 times more often ($p < 0.05$) as compared to patients of the 1st group, which was probably associated with an increased accumulation of unmetabolized liver products in COPD exacerbation phase.

Manifestations of dyspepsia in patients in group 2 also occurred more often as compared to patients in group 1 (1.7 times ($p<0.05$)), indicating impaired digestive processes due to the allocation of defective bile composition, probably accompanying colorectal dysbiosis due to repeated courses of COPD antibacterial therapy, the attachment to central mechanisms of anorexia and nausea as a result of hypoxia.

Feeling of heaviness or pain on palpation in the right hypochondrium was recorded in patients of the 2nd group

also with a frequency exceeding proper complain in patients of the 1st group by 2.5 times (p<0.05). There was no significant difference in the incidence of hepatomegaly in patients of groups 1 and 2 (p>0.05) (see Table 1).

Clinically, cholestasis syndrome was found in 28.8% of NASH patients of the 1st group and in 62.3% of patients of the 2nd group, which was manifested by itching of the skin, bitter taste in the mouth, and the presence of xanthomatous formations on the eyelids. In a small number of patients of the 1st group, splenomegaly was established (13.5%), however, in patients of the 2nd group, the frequency of splenomegaly exceeded mentioned parameter in the 1st group, respectively, by 2.7 times (p<0.05). The syndrome of endocrine disorders was observed in all NASH patients in the form of grade I obesity. At the same time, IGT was found more often in the presence of COPD by 2.1 times (see Table 1). Among the biochemical syndromes in the examined patients of group 2, cytolytic (100.0%), cholestatic (73.6%) was found, which exceeded the frequency in the 1st group by 2.3 times (p<0.05), mesenchymal inflammatory which occurred with a higher frequency as compared to group 1 by 1.9 times (p<0.05), and HCF syndrome (50.9%), which occurred with a higher frequency as compared to group 1 by 2.6 times (p<0.05). So, the incidence of major clinical and biochemical steatohepatitis syndromes in NASH patients with concomitant COPD in comparison with the isolated course of NASH increased significantly (p<0.05).

When analyzing biochemical syndromes in NASH, most often the increase in average liver activity alanine aminotransferase (ALT) indicators in blood serum was found, which in NASH without COPD was by 3.1 times higher as compared to apparently healthy humans (AHH) (p<0.05) and aspartate aminotransferase (AST) by 2.4 times (p<0.05) (Table 2). A significant decrease in the de Ritis factor (AST/ALT) was observed in 1.3 times (p<0.05), which, in the absence of positive markers of hepatitis B and C viruses in the serum, indicates non-alcoholic dysmetabolic and inflammatory liver disease. The confirmation of this fact were positive results of biochemical screening tests: SteatoTest and NASH-test (p<0.05) and negative results of ASH-test (p <0.05) in the examined patients, which excludes the alcoholic etiology of the disease.

In NASH patients with COPD, the cytolysis syndrome was more intense, since ALT activity exceeded in AHH by 3.8 times (p<0.05), and AST activity by 3.3 times (p<0.05), which led to a decrease in the de Ritis factor by 1.2 times (p<0.05) as compared to AHH (see table 2), since in addition to metabolic disorders in the pathogenesis of NASH and obesity in COPD conditions, it is likely to be involved the medication effects of drugs used in the treatment of exacerbation of COPD with hepatotoxicity [15].

The total bilirubin content in patients of group 2 exceeded the normative indexes by 1.9 times (p<0.05) as compared to 1.5 times in patients of group 1 (p<0.05). It should be noted that the level of total bilirubin in the blood of patients of group 2 increased due to an increase in both its fractions: conjugated — respectively by 2.3 times (p<0.05) versus 1.8 times (p<0.05) in 1 group, and unconjugated: excess by 1.8 times versus 1.3 times (p<0.05), respectively.

The presence of cholestasis syndrome was evidenced by the increase of alkaline phosphatase (ALP) activity by 1.4 times (p<0.05) in patients of 2nd group versus 1.2 times (p <0.05) in patients of group 1, activity γ-glutamyltransferase (γ-GT) — respectively by 1.3 vs. 1.2 times (p<0.05) (see Table 2).

Mild manifestations of insufficiency of the protein-synthesis function of the liver in comorbidity with COPD were found in 50.9% of patients in group 2 and 19.2% of patients in group 1 by reducing the average total protein content (in 1.3 times (p<0.05) only in patients in group 2) and the content of albumin in the blood (in 1.4 times in patients in group 2 (p<0.05)), in the 1st group there was only a tendency to decrease these parameter (p>0.05). The presence of mesenchymal-inflammatory syndrome in NASH patients in the 2nd group was indicated by hyperglobulinemia (in 1.5 times (p <0.05)), an increase in the thymol test (in the 1st group — in 1.3 times (p < 0.05), in the 2nd group — in 1.6 times (p <0.05)), as well as the decrease of the albumin-globulin coefficient (A/G coefficient) (in the 1st group — in 1.3 times (p <0.05), group 2 — in 2.1 times (p <0.05) (see Table 2), which is also due to exacerbation of COPD.

USG of the liver of the examined patients revealed a high frequency and probable degree of hepatomegaly (Table 1), medium-grained transformation of the structure and mosaic induration (hyperechogenicity, "heterogeneity") of the liver parenchyma due to its inflammation, as well as a significant degree of hepatic steatosis (a significant percentage of dorsal attenuation of the USG signal).

The examined patients observed statistically significant increase in HRI (p<0.001). Thus, the median and 25th and 75th quartile values for HRI in AHH were 1.12 (1.0–1.26), in the 1st group 1.93 (1.75–2.18), in the 2nd group — 2.46 (2.27–2.65). Analysis of OR by HRI in comparison groups (2 out of 1) indicates significant differences: OR=2.04 [CI 95% 1.11–3.76]. An increase in HRI is associated with the amount of lipid accumulation in the liver parenchyma, as evidenced by the direct statistically significant strong correlation between the degree of steatosis (according to SteatoTest) and HRI (r = 0.81; p <0.001). However, in NASH patients, in the background of obesity changes in liver echogenicity due to the presence of non-alcoholic steatosis have been associated with anthropometric and laboratory parameters. A direct statistically significant various power association was established between HRI and HOMA-IR (r=0.71; p<0.001), BMI (r=0.64; p<0.001), WC/HC (r=0.57; p<0.001), ALT (r=0.38; p<0.05), ALP (r=0.33; p<0.05), γ-GT (r=0.28; p<0.05), the content of triacylglycerols in the blood (r=0.51; p<0.001). At the same time, in NASH patients with COPD, the correlation matrix has changed somewhat: a direct statistically significant higher strength of the relationship is established between HRI and HOMA-IR (r=0.75; p<0.001), BMI (r=0,71; p<0.001), WC/HC (r=0.64; p<0.001), ALT (r=0.43; p<0.05), ALP (r=0.42; p<0, 05), γ-GT (r=0.45; p<0.05), blood triacylglycerol content (r=0.57; p<0.001).

To determine the diagnostic significance of HRI we used ROC analysis, according to which the growth of this indicator is an effective marker of diagnosis of NASH, in which the AUROC for HRI was 0.97 (95% CI 1.06–2.98; p<0.001).

The threshold for HRI diagnosed with NASH was calculated to be > 1.48 and the sensitivity, specificity, PPV and NPV were 93.8%, respectively; 100%; 100% and 73.9%. Analysis of the results of the diagnostic test for patients with a comorbid course of NASH and COPD indicates that AUROC for HRI was 0.99 (95% CI 1.18–3.24; p<0.001), and sensitivity and NPV increased in accordance with 96.8% and 87.8% at the calculated optimal HRI threshold value > 1.52. A moderate threshold increase was observed for HRI in parallel with increasing diagnostic value.

Conclusions. 1. Clinical course of non-alcoholic steatohepatitis with obesity and COPD comorbidity is characterized by higher frequency and intensity of clinical syndromes in comparison with NASH patients without COPD: astheno-vegetative (OR=2,05, 95% CI 1,09–3,88) abdominal pain (OR=2.59, 95% CI 1.17–5.71), portal hypertension (splenogamy, OR=2.16, 95% CI 1.03–6.87), cholestasis (OR=2.16, 95% CI 1.05–4.44).

2. The course of non-alcoholic steatohepatitis with obesity and COPD comorbidity is characterized by a higher incidence of biochemical syndromes as compared to NASH patients without COPD: mesenchymal inflammation (OR=1.88, 95% CI 1.02–3.49), cholestasis (OR=2,25, 95% CI 1,13–4,47), hepatocellular failure (decrease in albumin content, OR=2,65, 95% CI 1,17–6,02) and their intensity (p<0,05).

3. The comorbid course of NASH with COPD is characterized by a higher degree of hepatic steatosis (HRI, OR=2.04 [CI 95% 1.11–3.76]) compared to the group of NASH patients without COPD (p<0.05). and a higher diagnostic threshold for hepatorenal index, which correlates strongly with the degree of hepatic steatosis determined by the Steato-test (r=0.81; p<0.001).

The prospect of further research in this area is the development of effective treatments for patients with comorbid course of NASH and COPD on obesity background.

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