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THE STATE OF BLOOD LIPID SPECTRUM AND THE INDICATORS OF INSULIN RESISTANCE IN PATIENTS WITH NONALCHOLIC STEATOHEPATITIS WITH OBESITY AND HYPERTENSIVE DISEASE

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The study was aimed to find out the possible interaction of the blood lipid spectrum, the level of glycemia and the degree of insulin resistance on the clinical course of non-alcoholic steatohepatitis (NASH) on the background of obesity, depending on the presence of comorbid hypertensive disease (HD) II stage. The total of 90 patients with NASH were examined: of which 30 patients with NASH and obesity I degree (1 group), 30 patients with NASH and a comorbid flow of HD II stage and obesity I degree (group 2), 30 patients with HD II stage and obesity I degree (group 3). The studies of lipid spectrum in blood in patients with NASH showed results of the lipid spectrum of the blood and the insulin resistance degree in patients with non-alcoholic steatohepatitis and comorbidity with obesity and hypertension disease second degree. In patients with non-alcoholic steatohepatitis and obesity without accompanying hypertension, the following changes in the blood lipid profile are characteristic: the maximum increase in the content of triacylglycerol in the blood, the likely increase in the content of total cholesterol and low proatherogenic lipoproteins, the probable decrease in anti-atherogenic high-density lipoproteins, which, with the addition of the comorbid HDII stage it is likely to deepen, in addition to the indicator of hypertriacylglycerolemia. The reason for the progression of the metabolic syndrome against non-alcoholic steatohepatitis and hypertension is lipid distress syndrome with an increase in total blood cholesterol, low proatherogenic lipoprotein, and a deficiency of high-density anti-atherogenic lipoprotein.

Key words: nonalcoholic steatohepatitis, obesity, hypertonic disease, blood lipid spectrum, insulin resistance.

This work is a fragment of the research work "Pathogenetic mechanisms of mutual burden and clinical features of non-alcoholic fatty liver disease and chronic kidney disease, justification of differentiated treatment", registration number 0117U002351.

The comorbid flow of non-alcoholic steatohepatitis (NASH) and hypertensive disease (HD) on the background of obesity is often recently drawn to the attention of both practitioners and researchers [3,4,8]. Without correction of clinical and biochemical syndromes of liver damage by interrupting the cascade of interactions, the cessation of the progression of their inflammation, fibrosis of these organs and the restoration of their functional state can not be achived [7, 2, 9]. The dominant place in the pathogenesis of both diseases is the disturbance of carbohydrate and lipid homeostasis, nitrous oxide stress, endogenous intoxication, which promote acceleration of apoptosis of hepatocytes, endothelium, and further their cytolysis with the background of activation of autoimmune cytokine mechanisms of inflammation progression, fibrosing reactions, leading to progressive functional insufficiency of organs [8].

The purpose of the study was to find out the possible interaction of the blood lipid spectrum, the level of glycemia and the degree of insulin resistance on the clinical course of NASH on the background of obesity, depending on the presence of comorbid hypertensive disease II stage.

Material and methods of the research**.** 90 patients with NASH were examined: of which 30 patients with NASH and obesity I degree (1 group), 30 patients with NASH and a comorbid flow of HD II stage and obesity I degree (group 2), 30 patients with HD II stage and obesity II degree (group 3). To determine the dependence of NASH flow on the presence of HD, the group of patients was randomized according to age, sex, degree of obesity. The average age of patients was 43.2 ± 5.31 years. The compensation degree of carbohydrate metabolism was determined by the level of glycemia in the onset and two hours after glucose challenge (glucose tolerance test) by glucose oxidase method, blood intake of insulin onset (DRG System) - by ELISA, glycated hemoglobin blood count (HbA1c) using standard reagent kits "Danush Ltd" (Lviv). The degree of insulin resistance (IR) was determined by BMI: body weight (kg) / height^2 (m), ratio: waist circumference / hips; IR indices: glucose ratio (mmol / l) to insulin (μd / ml); the HOMA-IR index (D. R. Matthews) , which was calculated using the HOMA Calculator Version 2.2 Diabetes Trials Unit of the University of Oxford (UK). The lipid blood spectrum was studied in terms of the content of common lipids, TC, TG, LDL, and HDL in blood, using standard diagnostic sets of Danush Ltd (Lviv). The level of LPDH in the blood was calculated using the mathematical formula: the content of TG / 2.2. The index of atherogenicity (IA) was also calculated based on the ratio of the content of total TG / HDL-C.

The statistical analysis of the results was carried out in accordance with the type of research carried out and the types of numerical data that were obtained. Distribution normality was verified using Liliefors, Shapiro-Uilka tests and the direct visual evaluation of eigenvalues distribution histograms. Quantitative indices having a normal distribution are represented as mean (M) ± standard deviation (S). Discrete values are

presented in the form of absolute and relative frequencies (the percentage of observations to the total number of subjects surveyed). For comparisons of data that had a normal distribution pattern, parametric tests were used to estimate the Student's t-criterion, Fisher's F-criterion. In the case of abnormal distribution, the median test, Mann-Whitney Rank U-Score, and Wilcox's T-criterion (in the case of dependent groups) were used for multiple comparison. Statistica for Windows version 8.0 (Stat Soft inc., USA), Microsoft Excel 2007 (Microsoft, USA) software packages were used for statistical and graphical analysis of the obtained results.

Results of the study and their discussion. The studies of lipid spectrum in blood in patients with NASH showed a number of similar changes (Table 1), however, they differed in the degree of probability depending on the presence of the accompanying hypertensive disease. Thus, according to the concentration of total lipids in the blood of patients of groups 1 and 2 - the normal range exceeded by 26.3% and 34.3% respectively (p = 0.05), while in the third group, the minimum in compare with all groups - by 7.6% (p = 0.05) with the presence of a probable statistical difference between groups (p = 0.05). Blood content of the general TC also indicates its probable increase by 37.5% and 46.8% (p = 0.05) compared with the practiclly healthy persons in patients of the groups 1 and 2, the minimum excess in TC in patients 3rd group (by 13.0% (p = 0.05)). Probable changes in the concentration of TG in the form of a substantial increase (2.1 and 1.9 times, respectively (p = 0.05)) were recorded by us in the 1st and 2nd groups of patients, whereas in patients of 3rd group - changes were less significant (1.6 times, p = 0.05). That is, the TG content in blood with the comorbid flow of NASH with HD was probably lower than in patients with NASH without HD. The study of the concentrations of proatherogenic lipoprotein fractions in blood indicates a number of probable changes: LDL concentrations in patients in group 1 were significantly higher than the control index in 1.6 times (p=0.05), and patients of the groups 2 and 3 showed a probable growth of LDL in 1.8 and 1.5 times (p = 0.05), respectively, with a probable statistical difference between the groups (p=0.05). It should also be noted that with the increase in the activity of cytolysis, the content LDL and cholesterol decreased in patients with NASH, but due to comorbidity with HD - increased, which may be an important prognostic factor in the progression of atherosclerosis in these patients. Concentration in blood of antiatherogenic lipoproteins - HDL in patients of all groups was significantly lower in comparison with the control group (Table 1): in patients of the 1st group - in 1,6 times (p=0,05), in the 2nd group - in 1,8 times (p=0,05), in the 3rd group - 1,3 times (p=0,05).

Table 1

Indicators of blood lipid spectrum in patients with non-alcoholic steatohepatitis and obesity, depending on the presence of comorbid hypertonic disease and practically healthy persons (M ± m)

Indicators, units measurement	practically healthy persons, n=30	Groups of examined patients		
		NASH +obesity (Group 1), n=30	NASH + HD+obesity (Group 2), n=30	HD +obesity (Group 3), n=30
Total lipids, mmol/l	5,85±0,112	7,45±0,141 *	7,93±0,127 */**	6,35±0,130 */**/***
Total cholesterol, mmol/l	4,72±0,101	6,48±0,107 *	6,90±0,091 */**	5,31±0,116 */**/***
TG, mmol/l	1,47±0,033	3,15±0,018 *	2,73±0,009 */**	2,35±0,037 */**/***
LDL, mmol/l	2,59±0,028	4,25±0,037 *	4,59±0,024 */**	3,87±0,056 */**/***
HDL, mmol/l	1,29±0,048	0,83±0,012 *	0,70±0,011 *	0,96±0,023 */**/***

Notes: * - the difference is probable compared to the index in the practically healthy persons (p =0,05);** - the difference is probable in comparison with the index in patients with NASH (p <0,05);*** - the difference is probable compared with the index in patients with NASH with HD (p =0, 05).

As can be undersrood from the study results, the maximum suppression of HDL synthesis was observed in patients of the 2nd group, indicating a minimum level of vessels endothelium protection from free radical aggression and atherogenic fractions of blood lipids. The result of these changes was a significant increase in the index of atherogenicity in patients of all groups of observation: the 1st group - 2.2 times, the 2nd group - 2.7 times, the third group - 1.5 times (p = 0,05) (Table 1) with the maximum changes in the index in patients with NASH, HD and obesity, indicating on one hand the presence of significant risk factors for the progression of atherosclerosis in these patients with the background of obesity, and on the other - on the favorable pathogenetic situation with regard to the progression of NASH.

The results of glycemic indexes, insulinemia and insulin resistance indices in patients with isolated and comorbid HD and obesity with NASH are given in Table 2. The analysis of our performed studies showed that a slight increase in the level of fasting glycemia was found to be insignificant in patients 1 and 2, respectively by 9.4% and 14.7%, (p = 0.05) compared with the control group, while patients of the 3rd group, glycemic parameters were unlikely to see (Table 2). Analysis of postprandial glycemic parameters obtained during glucose tolerance test (GTT) in patients of groups 1 and 2 also showed an increase in glucose content after 120 minutes of loading - by 16.7% and 31.3% respectively (p = 0.05) in compared with the indicators in a practically healthy persons group, whereas in the 3rd group the changes were unlikely (p = 0.05). Investigation of insulin content in blood on an empty stomach revealed a probable hyperinsulinemia, which in patients with the 1st group exceeded the index in the a practically healthy persons group by 1.9 times; in patients of the 2nd group insulin content exceeded the norm by 2.2 times (p1-2 = 0,05) (Table 2).

Table 2

Indicators of glycemia and the degree of insulin resistance in the examined patients and practically healthy persons (M ± m)

Indicators, units measurement	Groups of examined patients			
	practically healthy persons, n=30	NASH+obesity, n=28 (Group 1)	NASH with HD+obesity, n=30 (Group2)	HD+obesity, n=20 (Group 3)
Glucose onset, mmol/l	5,11±0,117	5,59±0,104 *	5,86±0,112 *	5,25±0,095 ***
Glucose after 2 h, mmol/l	7,45±0,332	8,75±0,119 *	9,85±0,223 */**	7,73±0,241 **/***
Insulin, μU/ml	9,90±2,351	19,54±2,311*	21,57±2,426 *	11,85±0,242 **/***
HbA1c, %	5,07±0,135	5,59±0,101 *	5,65±0,114 *	5,09±0,145 **/***
HOMA-IR	1,30±0,163	2,61±0,019	2,80±0,037 */**	1,52±0,110**/***

Notes: * - the difference is probable compared to the index in the practically healthy persons (p =0,05);** - the difference is probable in comparison with the index in patients with NASH (p <0,05);*** - the difference is probable compared with the index in patients with NASH with HD (p =0, 05).

The presence of a perturbing sensitivity of peripheral tissues to insulin in patients with NASH and obesity indicates a probable increase in the HOMA IR index (by 2.0 and 2.2 times, respectively (p = 0.05), with a significant difference between the given groups (p = 0.05). In patients with NASH, on the background of obesity and HD, a maximum manifested IR syndrome was found, which is probably the primary (hereditary predisposition), and may be secondary to liver damage on the background of steatosis. The analysis results of the hemoglobin glycosylation degree study, as a marker of the duration of hyperglycemia episodes, showed a significant increase in the relative content of HbA1c in patients 1st and 2nd groups, which exceeded the index in a practiclly healthy person by 9.6% and 11.4% respectively (p=0,05), indicating the presence of latent hyperglycemia episodes (Table 2) in this contingent of patients. In patients with non-alcoholic steatohepatitis and obesity without accompanying hypertension is characterized by the following changes in the blood lipid spectrum: the maximum increase in the content of triacylglycerol in the blood (2.1 times, p=0.05), the likely increase in the content of total cholesterol (1.4 times, p=0,05) and low-density proatherogenic lipoproteins (1,6 times, p=0,05), the probable reduction of high-density anti-atherogenic lipoproteins (1,6 times, p =0,05), which with the addition to comorbid HD II Stage are likely to progress deeply (within 1.5-1.8 times, p=0.05), except for the indicator hypertriacylglycerolemia. The TG of blood index and the index of hepatocyte steatosis in patients with NASH on the background of obesity are believed to be higher (1.3 times (p=0.05)) (according to the steato-test: within S1-S2) from the indicators in patients with a comorbid flow of NASH, obesity and HD. For the comorbid flow of NASH and HD, the maximum growth of the index of atherogeny (2.7 times against 2.2 times in the isolated flow of NASH, p = 0.05) was established.

Conclusion

Consequently, the most significant metabolic prerequisites for the development of NASH on the background of obesity and HD are likely postprandial hyperglycemia, hyperinsulinemia, increased hemoglobin glycosylation, and primary tissue IR. The reason for the progression of the metabolic syndrome on the background of NASH and HD is a lipid distress syndrome with an increase in blood TG, proatherogenic LDL, deficiency of anti-atherogenic HDL. The leading role in the development and progression of steatohepatitis, disorders of the hepatic circulation results in an increase in blood TG. Thus, the development of NASH in patients with HD and obesity is accompanied by a significant disorder of hyperlipidemia with the highest among the groups comparing the increase in the content of cholesterol and low-density proatherogenic lipoproteins, the probable decrease in high-density anti-atherogenic lipoproteins and an increase in the atherogenicity index.

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Реферати

СТАН ЛІПІДНОГО СПЕКТРУ КРОВІ ТА ПОКАЗНИКІВ ІНСУЛІНОРЕЗИСТЕНТНОСТІ У ХВОРИХ НА НЕАЛКОГОЛЬНИЙ СТЕАТОГЕПАТИТ ІЗ ОЖИРІННЯМ ТА ГІПЕРТОНІЧНОЮ ХВОРОБОЮ

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Метою дослідження було з'ясування ймовірного взаємовпливу стану ліпідного спектру крові, рівня глікемії та ступеня інсулінорезистентності на клінічний перебіг неалкогольного стеатогепатиту (НАСГ) на тлі ожиріння залежно від наявності коморбідної гіпертонічної хвороби (ГХ) ІІ стадії. Обстежено 90 хворих на НАСГ: з яких 30 хворих на НАСГ із ожирінням І ступеня (1 група), 30 хворих на НАСГ із коморбідним перебігом ГХ ІІ стадії та ожирінням І ступеня (2 група), 30 хворих на ГХ ІІ стадії та ожирінням І ступеня (3 група). Результати дослідження та їх обговорення. Дослідження ліпідного спектру крові крові та ступеня інсулінорезистентності у пацієнтів з неалкогольним стеатогепатитом за коморбідності з ожирінням та гіпертонічною хворобою ІІ ст. супроводжується суттєвою дис- та гіперліпідемією із зростанням вмісту в крові холестеролу та проатерогенних ліпопротеїнів низької щільності, вірогідним зниженням протиатерогенних ліпопротеїнів високої щільності та зростанням індексу атерогенності. Причиною прогресування метаболічного синдрому на тлі неалкогольного стеатогепатиту та гіпертонічної хвороби, є ліпідний дистрес-синдром із зростанням у крові загального холестерину, проатерогенних ліпопротеїдів низької щільності, дефіцитом антиатерогенних ліпопротеїдів високої щільності.

Ключові слова: неалкогольний стеатогепатит, ожиріння, гіпертонічна хвороба, ліпідний спектр крові, інсулінорезистентність

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СОСТОЯНИЕ ЛИПИДНОГО СПЕКТРА КРОВИ И ПОКАЗАТЕЛЕЙ ИНСУЛИНОРЕЗИСТЕНТНОСТИ У БОЛЬНЫХ НЕАЛКОГОЛЬНОГО СТЕАТОГЕПАТИТА С ОЖИРЕНИЕМ И ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ

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Целью исследования было выяснение возможного влияния состояния липидного спектра крови, уровня гликемии и степени инсулинорезистентности на клиническое течение неалкогольного стеатогепатита (НАСГ) на фоне ожирения в зависимости от наличия коморбидной гипертонической болезни (ГБ) ІІ стадии. Обследовано 90 больных НАСГ: из которых 30 больных НАСГ с ожирением І степени (1 группа), 30 больных НАСГ с коморбидной ГБ ІІ стадии и ожирением І степени (2 группа), 30 больных ГБ ІІ стадии и ожирением І степени (3 группа). Результаты исследования и их обсуждение. Исследование липидного спектра крови и степени инсулинорезистентности у пациентов с неалкогольным стеатогепатитом за коморбидности с ожирением и гипертонической болезнью ІІ ст. сопровождается существенным дис- и гиперлипидемией с максимальным ростом в крови холестерина и проатерогенных липопротеинов низкой плотности, вероятным снижением протиатерогенных липопротеинов высокой плотности и ростом индекса атерогенности. Причиной прогрессирования метаболического синдрома на фоне неалкогольного стеатогепатита и гипертонической болезни является липидный дистресс-синдром с ростом в крови общего холестерина, проатерогенных липопротеидов низкой плотности, дефицитом антиатерогенных липопротеидов высокой плотности.

Ключевые слова: неалкогольный стеатогепатит, ожирение, гипертоническая болезнь, липидный спектр крови, инсулинорезистентность.

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CEPHALOMETRIC STUDIES OF UKRAINIAN BOYS AND GIRLS WITH ORTHOGNATHIC BITE BY THE METHOD OF R. M. RICKETTS

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According to literary sources, most of the cephalometric parameters obtained by the Ricketts method have age and gender differences, as well as significantly depend on the ethnicity and climatogeographical features of the region. That is why, before planning any orthodontic procedures, one cannot underestimate the cephalometric norms developed for different ethnic and age groups of the population. The purpose of the study is to establish and analyze the cephalometric parameters by the method of R.M. Ricketts in boys and girls of the Podillia region of Ukraine with orthognathic bite. Primary lateral teleroentgenograms of 38 young men and 55 girls with normal occlusion close to orthognathic bite, obtained using the Veraviewepocs 3D device, Morita (Japan), were taken from the data bank of the research center of the National Pirogov Memorial Medical University, Vinnytsya. Cephalometric measurements were performed according to the recommendations of R.M. Ricketts. Statistical processing of the obtained results was carried out in the licensed package "Statistica 6.0" using nonparametric methods for evaluating the obtained results. In analyzing the gender differences in cephalometric parameters obtained by the Ricketts method “Ricketts comprehensive computer description analysis” in boys with normal occlusion close to orthognathic bite, only for Canine Relation, Upper Molar Position, Upper Lip Length, Cranial Length - Anterior, Posterior Facial Height, Porion Location and Corpus Length. When comparing cephalometric parameters in boys and girls of Podillia with orthognathic bite with the magnitude of these parameters obtained by R. M. Ricketts, most indicators in both boys and girls have pronounced differences. Thus, the results obtained by us allow the orthodontist to predict both the growth and the changes obtained in the course of treatment of the parameters of the facial part of the head.

Key words: lateral teleroentgenograms of head, cephalometry, boys and girls Podillia with orthognathic bite, R. M. Ricketts analysis.

The requirement to equalize teeth in orthodontic patients remains not the most important problem in our time. Often, as a result of treatment, they want to get a good smile, which harmoniously corresponds to the correct features of the face [2, 10, 13]. In the process of growth and development of the tooth-jaw system, the upper and lower jaws in relation to the base of the skull move forward and downward. The upper jaw grows,