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Therapy

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CORRELATED INTERDEPENDENCES OF CHARACTERISTICS OF CARBOHYDRATE METABOLISM AND LIPID PROFILE AND BATOKINES LEVELS IN PATIENTS WITH CORONARY HEART DISEASE AND OBESITY

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Research of comorbid coronary heart disease (CHD) and obesity in recent years often rely on the study of inflammatory mediators, among which the first and foremost are batokines, in particular on fibroblast growth factor (FGF-21) and vascular endothelial growth factor A (VEGFa). The aim of our study was to determine the correlational interdependencies of indicators of carbohydrate metabolism and lipid profile and levels of batokines in the comorbidity of CHD and obesity. 70 people aged from 25 to 85 were examined with CHD on the background of obesity. The average age was (63.6±8.8) years. The research do not violate the principles of bioethics, which is confirmed by the conclusion of the Bioethics Committee of the Kharkiv National Medical University. All patients who participated in the study signed an informed voluntary consent. Based on the results of research probable direct strong correlations of total cholesterol (TC) with low-density lipoprotein (LDL) were determined (ρ=0.889; p=0.000); triglycerides (TG) with very low-density lipoprotein (VLDL) (ρ=0.810; p=0.000). The average strength of correlation was determined: glycosylated hemoglobin (HbA1c) with vascular endothelial growth factor A (VEGFA) (ρ=0.374; p=0.001); TC and LDL and AI (respectively ρ=0.615; p=0.000, and ρ=0.648; p=0.000); VLDL with atherogenic index (AI) (ρ=0.367; p=0.002). Probable direct weak correlations of blood glucose levels with TG (ρ=0.253; p=0.034) and VLDL (ρ=0.277; p=0.020) and VEGFA (ρ=0.225; p=0.061) were found; TG and VLDL with VEGFA (ρ=0.256; p=0.032 and ρ = 0.273; p = 0.022, respectively). Inverse interdependencies were recorded: medium strength – high-density lipoprotein (HDL) and AI (ρ=-0.583; p=0.000) and weak – hemoglobin levels with HDL (ρ=-0.251; p=0.036); HbA1c with LDL (ρ=-0.241; p=0.044); HDL with VLDL (ρ=-0.293; p=0.014).

Keywords: *comorbidity of coronary heart disease and obesity, batokines, FGF21, VEGFA.*

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Introduction

Many studies confirm the significant spread and growth of non-communicable diseases (NCDs). NCDs are the main cause of disability in the world population and mortality (73.4% of all deaths). Specialists of George Washington University determined that the leading causes of death among 108 countries are: arterial hypertension, tobacco smoking, overweight and obesity, hunger and malnutrition, diabetes, excessive salt consumption, environmental factors, increased blood cholesterol levels and alcohol abuse [1]. According to the World Health Organization (WHO), European countries have 60.0% of total Disability-adjusted life years (DALYs) due to the main seven risk factors, among which NCDs take the first place: 77.0% – NCDs; 14.0% – external causes, injuries and poisoning; 12.8% – arterial hypertension; 12.3% – smoking; 10.1% – alcohol abuse; 9.0% – infectious diseases; 8.7% – increased levels of blood cholesterol; 7.8% – overweight and obesity; 4.4% – insufficient consumption of vegetables and fruits and 3.5% – a sedentary lifestyle. NCDs in European countries each year cause 86.0% of the 9.6 million total deaths and account for 77.0% of the 150.3 million DALYs.

Among all NCDs in terms of prevalence and causes of death and disability of the population, cardiovascular diseases (CVD) take the first place, among which coronary heart disease (CHD) is the most common cause of death and disability among all CVDs [2]. These conclusions are supported by the results of GBD studies [3], according to which the double burden of diseases caused by NCDs and infectious diseases is currently recorded.

Official WHO statistics indicate that the main cause of mortality is CHD (16.0% of all global deaths), the death rate from which has recently increased by 2 million (up to 9 million) per year [4].

It is determined that the main pathogenetic mechanism of the development of CVD is the appearance of atherosclerotic vascular lesions, due to which CHD develops in the majority of cases. The main etiological factors of the development of CVD are hyperlipidemia, blood pressure, diabetes, obesity, alcohol abuse, and low physical activity [5–8]. The main factor is CHD, especially due to its comorbidity with obesity [8].

In recent years, the attention of scientific research in the direction of determining the features of the comorbid course of CHD and obesity has been directed to the study of inflammatory mediators, among which the first and foremost are batokines (fibroblast growth factor – FGF-21 and vascular endothelial growth factor A – VEGFa), which are produced in these diseases.

Therefore, the study of the correlational interdependencies of the characteristics of carbohydrate metabolism and lipid profile with indicators of batokine metabolism in CHD and obesity is a very relevant and significant problem.

The aim of the research was to determine the correlational interdependencies of indicators of carbohydrate metabolism and lipid profile and levels of batokines in the comorbidity of CHD and obesity.

Materials and Methods

130 people aged from 25 to 85 were examined with CHD on the background of obesity. The average age was (63.6±8.8) years. The research does not violate the principles of bioethics (which is confirmed by the conclusion of the Bioethics Committee of the Kharkiv National Medical University). All examined patients signed a voluntary informed consent.

The criteria for inclusion in the study group were: 18 years of age, presence CHD on the background of obesity, signed informed consent for voluntary participation in the study. Exclusion criteria were: age less than 18 years, absence CHD and

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obesity, presence: diffuse and focal diseases, endocrine pathology, allergic reactions, diseases of internal organs, the presence of severe decompensated somatic pathology, the presence of mental and oncological diseases, pregnancy, chronic alcoholism, refusal to participate in our study and refusal to comply with all prescriptions.

The diagnosis of CHD was established according to current guidelines [9]. The diagnosis of obesity was determined according to the recommendations of the European Association for the Study of Obesity (2017) [10].

Determination of indicators of batokines was carried out using generally accepted methods.

When conducting medical-statistical calculations, the distribution of signs (qualitative and quantitative) was carried out graphically visually and using the normality test of Kolmogorov-Smirnov and Lilliforce and Shapiro-Wilk. The presence of significant differences from the normal nature of the distribution was determined. The following calculations were carried out using non-parametric medical and statistical methods.

The relationship between the obtained parameters was determined using the Spearman Rh_o rank correlation coefficient. If Rh_o was in the range from 0 to -1.0, the correlation was defined as inverse; if from 0 to 1.0 – a straight line. Rh_o from 0 to 0.3 (from 0 to -0.3) was characterized as a weak relationship between traits; from 0.4 to 0.7 (from -0.4 to -0.7) – moderate and from 0.7 to 1.0 (from -0.7 to -1.0) – significant. The result was presented as the value of the Rho coefficient and the corresponding confidence level p.

The threshold value of the probability level of all calculated features was taken at the level of 0.05 (p=0.05). Statistical calculations were performed using IBM SPSS 25.0 for Windows (USA).

Results and Discussion

An analysis of the correlational interdependencies of the characteristics of carbohydrate metabolism and lipid profile and the levels of batokines in patients with CHD and obesity was carried out. Were analyzed correlations of hemoglobin, glycosylated hemoglobin (HbA1c), blood glucose, total cholesterol (TC), high-density lipoprotein (HDL), triglycerides (TG), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), atherogenic index (AI) and batokines (FGF21 and VEGFA) (*Table*).

There were probable weak inverse correlations of hemoglobin levels with HDL values (ρ=-0.251; p=0.036) and at the limit of probability – with LDL indicators (ρ=-0.207; p=0.086) and improbable weak direct correlations – with HbA1c (ρ=0.024; p=0.844) and blood glucose (ρ=0.201; p=0.095), levels of TG (ρ=0.201; p=0.096) and VLDL (ρ=0.135; p=0.265) and FGF21 (ρ=0.114; p=0.346) and unlikely weak inverses – with TC (ρ=-0.199; p=0.099) and AI (ρ=-0.017; p=0.890) values and VEGFA levels (ρ=-0.012; p=0.922) (*Table*).

HbA1c indicators had a probable direct correlation of medium strength with VEGFA levels (ρ=0.374; p=0.001) and a weak correlation with blood glucose characteristics (ρ=0.303; p=0.011) and a weak inverse correlation with LDL parameters (ρ=-0.241; p=0.044). Improbable correlations were noted: weak direct correlations with HDL (ρ=0.023; p=0.850) and TG (ρ=0.097; p=0.423) and VLDL (ρ=0.070; p=0.563) and FGF21 (ρ=0.132; p=0.277) and weak reverse – with the characteristics of TC (ρ=-0.192; p=0.111) and AI (ρ=-0.179; p=0.138) (*Table*).

Probable, blood glucose levels had weak direct correlations with the characteristics of TG (ρ=0.253; p=0.034) and VLDL (ρ=0.277; p=0.020) and VEGFA (ρ=0.225; p=0.061) and improbable weak

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Table. Correlational interdependencies of characteristics of carbohydrate metabolism and lipid profile and levels of batokines in subjects with CHD and obesity

Characteristics		Hemoglobin, g/l	HbA_{1c}, %	Glucose, mmol/l	TC, mmol/l	HDL, mmol/l	TG, mmol/l	LDL, mmol/l	VLDL, mmol/l	AI	FGF21, pg/ml	VEGFA, pg/ml
Hemoglobin, g/l	ρ	1,000	0,024	0,201	-0,199	-0,251	0,201	-0,207	0,135	-0,017	0,114	-0,012
	p	–	0,844	0,095	0,099	0,036	0,096	0,086	0,265	0,890	0,346	0,922
HbA_{1c}, %	ρ	0,024	1,000	0,303	-0,192	0,023	0,097	-0,241	0,070	-0,179	0,132	0,374
	p	0,844	–	0,011	0,111	0,850	0,423	0,044	0,563	0,138	0,277	0,001
Glucose, mmol/l	ρ	0,201	0,303	1,000	0,114	0,011	0,253	0,002	0,277	0,059	0,167	0,225
	p	0,095	0,011	–	0,349	0,929	0,034	0,985	0,020	0,630	0,167	0,061
TC, mmol/l	ρ	-0,199	-0,192	0,114	1,000	0,236	0,085	0,889	0,169	0,615	-0,019	0,118
	p	0,099	0,111	0,349	–	0,049	0,486	0,000	0,161	0,000	0,874	0,333
HDL, mmol/l	ρ	-0,251	0,023	0,011	0,236	1,000	-0,159	0,104	-0,293	-0,583	-0,118	-0,120
	p	0,036	0,850	0,929	0,049	–	0,190	0,391	0,014	0,000	0,332	0,324
TG, mmol/l	ρ	0,201	0,097	0,253	0,085	-0,159	1,000	-0,190	0,810	0,199	0,175	0,256
	p	0,096	0,423	0,034	0,486	0,190	–	0,115	0,000	0,099	0,146	0,032
LDL, mmol/l	ρ	-0,207	-0,241	0,002	0,889	0,104	-0,190	1,000	-0,124	0,648	-0,078	-0,038
	p	0,086	0,044	0,985	0,000	0,391	0,115	–	0,307	0,000	0,521	0,756
VLDL, mmol/l	ρ	0,135	0,070	0,277	0,169	-0,293	0,810	-0,124	1,000	0,367	0,200	0,273
	p	0,265	0,563	0,020	0,161	0,014	0,000	0,307	–	0,002	0,097	0,022
AI	ρ	-0,017	-0,179	0,059	0,615	-0,583	0,199	0,648	0,367	1,000	0,004	0,130
	p	0,890	0,138	0,630	0,000	0,000	0,099	0,000	0,002	–	0,971	0,283
FGF21, pg/ml	ρ	0,114	0,132	0,167	-0,019	-0,118	0,175	-0,078	0,200	0,004	1,000	0,520
	p	0,346	0,277	0,167	0,874	0,332	0,146	0,521	0,097	0,971	–	0,000
VEGFA, pg/ml	ρ	-0,012	0,374	0,225	0,118	-0,120	0,256	-0,038	0,273	0,130	0,520	1,000
	p	0,922	0,001	0,061	0,333	0,324	0,032	0,756	0,022	0,283	0,000	–

direct correlations – with values of TC (ρ=0.114; p=0.349) and HDL (ρ=0.011; p=0.929), levels of LDL (ρ=0.002; p=0.985) and AI (ρ=0.059; p=0.630) and characteristics of FGF21 (ρ=0.167; p=0.167). TC values were probably quite strongly directly correlated with LDL (ρ=0.889; p=0.000) and moderately strongly with AI characteristics (ρ=0.615; p=0.000) and had implausible weak direct correlations with HDL levels (ρ=0.236; p=0.049) and TG (ρ=0.085; p=0.486) and with the values of VLDL (ρ=0.169; p=0.161) and VEGFA (ρ=0.118; p=0.333) and inverse interdependencies – with the levels of FGF21 (ρ=-0.019; p=0.874) (*Table*).

HDL levels were only weakly inversely correlated with LDL (ρ=-0.293; p=0.014) and moderately strongly correlated with AI characteristics (ρ=-0.583; p=0.000) and had weak improbable direct correlations with LDL (ρ=0.104; p=0.391) and inverse interdependencies – with the levels of TG (ρ=-0.159; p=0.190) and batokines (FGF21 – ρ =-0.118; p =0.332; and VEGFA – ρ=-0.120; p=0.324). TG was likely directly weakly correlated with VEGFA values (ρ=0.256; p=0.032) and quite strongly with VLDL levels (ρ=0.810; p=0.000) and had unlikely weak direct correlations with AI characteristics (ρ=0.199; p=0.099) and FGF21 (ρ=0.175; p=0.146)

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and inverse interdependencies – with LDL indicators (ρ=-0.190; p=0.115) (*Table*).

Registered probable medium-strength direct correlations of LDL and AI values (ρ=0.648; p=0.000) and improbable low-strength inverse correlations of LDL and VLDL (ρ=-0.124; p=0.307) and batokines (FGF21 – ρ=-0.078; p=0.521 and VEGFA – ρ=-0.038; p=0.756). VLDL characteristics were directly weakly correlated with VEGFA levels (ρ=0.273; p=0.022) and moderately strongly with AI characteristics (ρ=0.367; p=0.002) and had improbable weak correlations with FGF21 levels (ρ=0.200; p=0.097) (Table).

AI values had only implausible weak correlations with the levels of batokines (FGF21 – ρ=0.004; p=0.971; and VEGFA – ρ=0.130; p=0.283), and FGF21 levels were expected to be moderately strongly correlated with VEGFA levels (ρ=0.520; p=0.000).

The results of our research on the existence of correlational interdependencies between batokines and carbohydrate metabolism and lipid profile characteristics are fully confirmed by other studies. Babak O.Y. and Lapshyna K.A. [12] the presence of correlations between FGF-21 and indicators of the metabolic profile has been proven. A weak direct relationship between FGF-21 and lipid profile indicators was found: r=+0.41 with TC, r=+0.36 – TG, r=+0.44 – LDL, r=+0.34 – VLDL, r=+0.42 with AI (p=0.001); and carbohydrate metabolism: r=+0.48 with glucose. An inverse weak correlation was determined between the level of FGF-21 and HDL – r=-0.39 (p=0.001).

Conclusions

Thus, when studying the correlational interdependencies of indicators of carbohydrate metabolism and lipid profile and levels of batokines in the comorbidity of coronary artery disease and obesity, it was probable direct strong correlations of TC with LDL were determined (ρ=0.889; p=0.000); TG with VLDL (ρ=0.810; p=0.000). The average strength of correlation was determined: HbA1c with VEGFA (ρ=0.374; p=0.001); TC and LDL and AI (respectively ρ=0.615; p=0.000 and ρ=0.648; p=0.000); VLDL with AI (ρ=0.367; p=0.002). Probable direct weak correlations of blood glucose levels with TG (ρ=0.253; p=0.034) and VLDL (ρ=0.277; p=0.020) and VEGFA (ρ=0.225; p=0.061) were found; TG and VLDL with VEGFA (ρ=0.256; p=0.032 and ρ=0.273; p=0.022, respectively). Inverse interdependencies were recorded: medium strength – HDL and AI (ρ=-0.583; p=0.000) and weak – hemoglobin levels with HDL (ρ=-0.251; p=0.036); HbA1c with LDL (ρ=-0.241; p=0.044); HDL with VLDL (ρ=-0.293; p=0.014).

Conflict of interest is absent.

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Гріднєва О.В.

КОРЕЛЯЦІЙНІ ВЗАЄМОЗАЛЕЖНОСТІ ХАРАКТЕРИСТИК ВУГЛЕВОДНОГО ОБМІНУ ТА ЛІПІДНОГО ПРОФІЛЮ І РІВНІВ БАТОКІНІВ ХВОРИХ ПРИ ІШЕМІЧНІЙ ХВОРОБІ СЕРЦЯ ТА ОЖИРІННІ

В статті визначено кореляційні взаємозалежності показників вуглеводного обміну та ліпідного профілю і рівнів батокінів при ішемічній хворобі серця (ІХС) та ожирінні, що і було визначено метою нашого дослідження. Обстежено 70 хворих у віці від 25 до 85 років з ІХС на фоні ожиріння. Середній вік пацієнтів склав (63,6±8,8) роки. Дослідження не порушує принципів біоетики, що підтверджено висновком комісії Харківського національного медичного університету. Усі пацієнти підписали інформовану згоду на добровільну участь у дослідженні. За результатами досліджень вірогідно визначено вірогідні прямі сильні кореляції загального холестерину (ЗХ) із ліпопротеїнами низької щільності (ЛПНЩ) (ρ=0,889; p=0,000); тригліцеридів (ТГ) із ліпопротеїнами досить низької щільності (ЛПДНЩ) (ρ=0,810; p=0,000). Визначені середньої сили кореляції: глікозильованого гемоглобіну (HbA1c) із рівнями фактору росту ендотелію судин А (VEGFA) (ρ=0,374; p=0,001); ЗХ і ЛПНЩ і коефіцієнтом атерогенності (КА) (відповідно ρ=0,615; p=0,000 і ρ=0,648; p=0,000); ЛПДНЩ із КА (ρ=0,367; p=0,002). Констатовані вірогідні прямі слабкі кореляції глюкози крові з ТГ (ρ=0,253; p=0,034) і ЛПДНЩ (ρ=0,277; p=0,020) та VEGFA (ρ=0,225; p=0,061); ТГ і ЛПДНЩ із VEGFA (відповідно ρ=0,256; p=0,032 і ρ=0,273; p=0,022). Зафіксовані зворотні кореляції: середньої сили –

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ліпопротеїнів високої щільності (ЛПВЩ) і КА (ρ=-0,583; p=0,000) та слабкі – рівнів гемоглобіну з ЛПВЩ (ρ=-0,251; p=0,036); HbA1c із ЛПНЩ (ρ=-0,241; p=0,044); ЛПВЩ із ЛПДНЩ (ρ=-0,293; p=0,014).

Ключові слова: *коморбідність ішемічної хвороби серця та ожиріння, батокіни, FGF21, VEGFA.*

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