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CHANGES IN METABOLIC PARAMETERS IN ISCHEMIC HEART DISEASE AGAINST THE BACKGROUND OF METABOLIC SYNDROME

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For many years, and to this day, cardiovascular disease has been and remains the leading cause of death worldwide. Cardiovascular diseases mainly affect people in countries with middle and low living standards.
The aim *of the study was to find out the peculiarities of lipid, carbohydrate, and hormonal changes in patients with coronary heart disease against the background of metabolic syndrome.*
Materials and methods: *120 patients with verified coronary heart disease were examined, including 60 patients with coronary heart disease without metabolic syndrome and 60 patients with coronary heart disease with metabolic syndrome. The control group consisted of 30 practically healthy individuals of appropriate age and sex. The content of HbA1c, glucositol C-peptide, triacylglycerols, total cholesterol, leptin, HDL-cholesterol, and LDL-cholesterol in blood serum was determined by modern methods.*
Results: *The analysis of the results of laboratory tests of patients' blood revealed more pronounced changes in carbohydrate and lipid metabolism in patients with coronary artery disease against the background of metabolic syndrome, which indicates the severity of the clinical course in such patients. The results obtained indicate that in coronary heart disease with metabolic syndrome, there are more pronounced dysmetabolic changes: hyperleptinemia, glucosemia, elevated HbA1c, and decreased C-peptide content. Studies have shown that obesity is accompanied by high levels of leptin, which exacerbates insulin resistance and is a trigger for the development of coronary heart disease.*
Conclusions: *1. Leptin resistance is a potential cause of insulin resistance and, consequently, obesity, which ultimately leads to metabolic syndrome and the development of coronary heart disease. The data obtained indicate a greater tendency to obesity in women with coronary heart disease complicated by metabolic syndrome.*
2. The data obtained may indicate a latent disorder of carbohydrate metabolism in patients with coronary artery disease without metabolic syndrome.
3. The detected deviations in lipid metabolism indicate the presence of type II dyslipoproteinemia in patients of group 1 and type IV dyslipoproteinemia in patients of group 2
Keywords: *ischemic heart disease, metabolic syndrome, diabetes, leptin, glucose, glycated Hb, C-peptide, cholesterol, triacylglycerols, HDL-cholesterol, LDL-cholesterol*

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1. Introduction

For many years and to this day, cardiovascular diseases have been and remain the leading cause of death worldwide. Cardiovascular diseases mainly affect people in countries with middle and low standards of living and depend on many factors: gender [1], Lifestyle [2], and the state of the microbiome [3].

Atherosclerosis and cardiovascular diseases, particularly coronary heart disease (CHD), have common developmental factors. The main factors for the development and progression of CHD and atherosclerosis include physical inactivity, overweight, dyslipidemia, smoking, excessive alcohol consumption, insulin resistance, hyperglycaemia, hypertension, male gender, thrombogenic factors, and hereditary predisposition [3, 4]. When these factors are combined, their mutual influence on each other increases, which in turn dramatically increases the risk of developing these nosologies [5–7].

The aim of the study was to find out the peculiarities of lipid, carbohydrate metabolism, and hormonal changes in patients with coronary heart disease against the background of metabolic syndrome (MS).

2. Materials and methods

120 patients with verified CHD were examined, including 60 patients with CHD without MS (group 1: .30 men, 30 women) and 60 patients with coronary heart disease with MS (group 2: 29 men, 31 women). The average age of the patients was 50±5 years. The control group consisted of 30 practically healthy individuals of the appropriate age and gender. Patients with CHD (with metabolic syndrome and without metabolic syndrome)

were treated at Lviv communal city clinical emergency medical hospital, Ukraine, during 2019–2021 years.

The research was carried out taking into account safety measures for the health of patients, respecting their rights, human dignity and moral and ethical norms following the principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine and the relevant Laws of Ukraine. This study was approved by the Ethical Committee of the Danylo Halytsky Lviv National Medical University, Ukraine (meeting minutes No. 2 dated February 15, 2019), and written informed consent was obtained from patients if they agreed to blood sampling.

The content of glycated haemoglobin (Hb A1c) was determined by the colourimetric method, and the content of glucose and C-peptide was determined by the enzymatic method using an automatic analyzer COBAS INTEGRA 400 plus. Triacylglycerols (TG) and total cholesterol were determined by the colourimetric enzymatic method (GPO-PAP) [8]. Leptin levels were determined by enzyme-linked immunosorbent assay. The "gender" leptin index (GLI) was calculated as the ratio of leptin levels in women and men in the control group and in pathology.

To detect the level of HDL-C and LDL-C, an enzymatic colour test was performed (HDL Cholesterol liquicolor and LDL Cholesterol liquicolor by HUMAN). The atherogenic coefficient (AC) was calculated using the formula AC = (total cholesterol - HDL-C) / HDL-C.

Statistical processing of the results was carried out using the data obtained using the methods of mathematical statistics using the program STATISTICA 8.0 (StatSoft, USA) [9]. The results are presented as mean and standard deviation. Values at $p<0.05$ were considered significant.

3. Results

The analysis of the results of laboratory tests of patients' blood revealed significant differences in the indicators of different groups (Table 1).

According to the results of the study, the level of leptin in group 1 was significantly higher than that of the control group in women by 16 % ($p<0.05$) and in men by 22 % ($p<0.05$). Leptin levels in patients of group 2 exceeded those of the control group in women by 5.5 times ($p<0.05$) and in men by 4 times ($p<0.05$). Indicators of group 2 exceeded the level of leptin in group 1: 4.6 times in women and 3 times in men ($p<0.05$).

Table 1

Indicators of carbohydrate metabolism in patients with coronary heart disease and coronary heart disease with metabolic syndrome (M±m)

Control group, n=30		Patient groups			
		Group 1, (n=60)		Group 2, (n=60)	
Leptin (ng/ml)					
women	men	women	men	women	men
7.4±0.8	3.8±0.3	8.8±0.8*	4.85±0.4	40.85±3.7*#	14.87±1.7*#
Gender leptin index (GLI)					
1.95±0.15		1.81±0.10		2.75±0.20	
Glucose (mmol/l)					
3.8±0.1		5.88±0.19*		6.63±0.10*#	
Glycated Hb (%)					
4.1±0.2		6.44±0.17*		6.50±0.9*	
C-peptide (ng/ml)					
3.20±0.24		1.17±0.10*		1.02±0.1*#	

*Note: * – significance of difference compared with the control group ($p<0.05$); # – significance of difference compared with group 1 with CHD ($p<0.05$)*

GLI in group 1 was 1.81±0.10, which was not statistically significantly different from the control value (1.95±0.15; $p>0.05$). In group 2, the GLI was 2.75±0.20, which was statistically significantly higher than the control value by 41 % and 52 % higher than the GLI of group 1 ($p<0.05$).

The plasma glucose content in patients with CHD exceeded the normal values by 35 % ($p<0.05$) but was within the reference values. In patients with CHD against the background of MS, the glucose content exceeded the control by 43 % ($p<0.05$). There was also a significant difference between the indicators in the groups of patients ($p<0.05$): the indicators of patients in the group of patients with CHD were 19 % lower than those with complications of MS ($p<0.05$).

The content of Hb A1c in the blood of patients with CHD and MS exceeds the control by 58 % ($p<0.05$), and this indicator does not differ statistically between the groups ($p>0.05$). In our study, we found a 2.7-fold decrease in C-peptide in the blood of patients in group 1 and 3.1-fold in group 2 ($p<0.05$). A more pronounced decrease in C-peptide in group 2 by 15 % ($p<0.05$) was found between the groups of patients.

The analysis of the results of laboratory blood tests revealed significant differences in lipid metabolism in patients of different groups (Table 2).

Table 2

Indicators of lipid metabolism in patients with coronary heart disease and coronary heart disease with metabolic syndrome, (M±m)

Control group, (n=30)	Patient groups	
	Group 1, (n=60)	Group 2, (n=60)
Cholesterol, (mmol/l)		
3.70±0.12	3.5±0.10	4.74±0.09*#
TG, (mmol/l)		
1.0±0.09	1.76±0.05	2.64±0.12*#
HDL-C, (mmol/l)		
1.62±0.08	1.11±0.05*	0.90±0.03*
LDL-C (mmol/l)		
2.16±0.13	2.57±0.10*	2.92±0.12*#
AC		
0.96±0.10	2.15±0.12*	3.74±0.22*#

*Note: * – significance of difference compared with the control group (p<0.05); # – significance of difference compared with group 1 with coronary heart disease (p<0.05)*

The content of total cholesterol in the blood serum of patients of group 1 does not exceed the normal values (p>0.05); in patients of group 2, the level of cholesterol exceeds the normal values by 28 % (p<0.05), and the indicators of group 1 patients by 35 % (p<0.05).

In patients with CHD and with complications of MS, the average cholesterol level is within the reference values. However, in group 2, the cholesterol content exceeds the control values by 28 % and the index of group 1 by 35 % (p<0.05).

The content of triacylglycerols in the blood serum of patients in group 1 significantly exceeds the normal values by 1.75 times (p<0.05); in patients in group 2, the level of TG exceeds the normal values by 2.6 times, and the indicators of group 1 by 1.5 times (p<0.05).

The content of HDL-cholesterol in the blood serum was reduced in patients of both groups by 1.6 times compared to the control group. The content of LDL-cholesterol in the blood serum of patients in group 1 exceeds the control group by 19 % (p<0.05); in patients in group 2, the content of LDL-cholesterol exceeds the control by 35 %, and the indicators of group 1 by 14 % (p<0.05).

The integral index characterizing lipid metabolism is the atherogenicity coefficient (AC). We found a significant excess of the control index of CA in group 1 by 2.2 times, in group 2 by 4 times (p<0.05), AC in group 2 exceeded the index in group 1 by 1.5 times (p<0.05).

4. Discussion

The data obtained indicate a more pronounced hyperleptinemia in women and, as a result, a greater tendency to obesity, which significantly complicates the clinical manifestations and course of many diseases, including coronary heart disease. Detected hyperleptinemia in metabolic syndrome closes a vicious circle that leads to clinical manifestations [10, 11].

Detected hyperglycaemia in patients with metabolic syndrome is one of the pathological factors that make up the vicious circle of cardiovascular disease. A one-time determination of blood glucose in patients does not give an idea of the state of carbohydrate metabolism, especially when the disorders are hidden.

One of the most important indicators of carbohydrate metabolism is the content of insulin, a hormone that regulates glycaemia and ensures the penetration of glucose into cells. In laboratory practice, the determination of the concentration of C-peptide is used to show the amount of endogenous insulin [12].

It is the elevated level of triacylglycerols that indicates the presence of obesity as the main clinical sign of metabolic syndrome and indicates a violation of lipid metabolism. Elevated triacylglycerol levels are a risk factor for atherosclerosis, coronary syndrome, and coronary heart disease.

Lipoproteins are an important transport form of lipids. Disturbances in the ratio of different classes of lipoproteins are called dyslipoproteinemia. Determination of the type of dyslipoproteinemia allows to diagnose a number of diseases.

Reduced serum HDL cholesterol indicates a reduced level of phospholipids, the only anti-atherogenic lipid fraction. This class of lipoproteins transports cholesterol from peripheral tissue cells to the liver. The LDL-cholesterol class in the blood serum contains the vast majority of circulating cholesterol and transports it to peripheral tissue cells. In cells, cholesterol is used for synthetic processes. The detected abnormalities in lipid metabolism indicate the presence of type II dyslipoproteinemia in patients of group 1 and type IV dyslipoproteinemia in patients of group 2.

Thus, more pronounced changes in carbohydrate and lipid metabolism were found in patients with coronary artery disease against the background of metabolic syndrome, which indicates the severity of the clinical course in such patients.

The results obtained indicate that in CHD with metabolic syndrome, there are more pronounced dysmetabolic changes: hyperleptinemia, glucosemia, elevated Hb A1c, and reduced C-peptide content. Studies have shown that obesity is accompanied by high levels of leptin, which exacerbates insulin resistance and is a trigger for the development of CHD.

Limitations of our study: Most patients in the present study had poor glycemic control. An accurate relationship between lipid metabolism indices and coro-

nary heart disease against the background of metabolic syndrome can be made out with logistic regression analysis. This requires a larger sample of studies.

Prospects for further research. Further study of age and gender characteristics of coronary heart disease against the background of metabolic syndrome.

5. Conclusions

1. Leptin resistance is a potential cause of insulin resistance and, consequently, obesity, which ultimately leads to metabolic syndrome and the development of CHD. The data obtained indicate a greater tendency to obesity in women with CHD complicated by MS.

2. The data obtained may indicate a latent disorder of carbohydrate metabolism in patients with CHD without MS.

3. The detected deviations in lipid metabolism indicate the presence of type II dyslipoproteinemia in patients of group 1 and type IV dyslipoproteinemia in patients of group 2.

Conflict of interest

The authors declare that there is no financial, personal, authorial or other conflict of interest that could affect the research and its results presented in this article.

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Data availability

Data will be made available on reasonable request.

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