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Changes in Lipid Metabolism in Patients with Ischemic Heart Disease Associated with Intestinal Dysbiosis

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Abstract

Mortality from cardiovascular diseases (CVD) currently occupies one of the leading positions. The main diseases that cause death are coronary heart disease (CHD). In the course of a retrospective study, the medical histories of 167 patients with chronic CHD were analyzed. The experiment included women aged 47-55 years with a history of information about the presence of disorders from lipid metabolism and intestinal dysbiosis of varying degrees. Thus, in patients with coronary heart disease against the background of intestinal dysbiosis of III-IV degrees, significant lipid metabolism disorders associated with an increase in cholesterol, LDL and TG are observed. Based on the data obtained on the absence of significant changes in liver tests, it can be concluded that the leading role of the exogenous lipid intake pathway is in the formation of dyslipidemia.

Discipline: Medicine (Cardiology).

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1 Introduction

Mortality from cardiovascular diseases (CVD) currently occupies one of the leading positions [1]. The main disease that leads to a fatal outcome is coronary heart disease (CHD) [2]. A large number of factors participate in the development of coronary artery disease, among which stenosing atherosclerosis of the coronary arteries is the leading one [3,4]. In approximately 88% of cases, patients with coronary heart disease had previously had lipid metabolism disorders [5]. According to recent studies [6-8], a disposing factor in the development of lipid metabolism disorders is disorders of the gastrointestinal tract (gastrointestinal tract) due to a violation of the balance between normal and pathological intestinal flora – dysbiosis. The exact mechanisms of participation of representatives of the microflora of the human body and their waste products in the development of atherosclerosis and other diseases associated with elevated cholesterol levels have not been fully studied [9].

The main links of cholesterol biosynthesis are acetate – cholesterol – fatty acids – sex hormones. At the first stage of this process, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) is synthesized from three molecules of acetate and coenzyme A. Further, as a result of the action of the enzyme HMG-CoA reductase, mevalonic acid is formed, which after about 20 subsequent stages turns into cholesterol [10,11].

2 Literary Review

Despite the complexity and multi-stage nature of these processes, the key enzyme determining the rate of cholesterol synthesis is HMG-CoA reductase. The intracellular cholesterol content is regulated by two mechanisms. The first of them controls the production of cholesterol by a negative feedback mechanism. The second mechanism for controlling the level of cholesterol in the cell is associated with the regulation of its transport through the cell membrane from the intercellular space. This transport is carried out with the participation of low-density lipoprotein receptors [8,12].

Dozens of enzymes are involved in cholesterol metabolism, and a mutation in each of the genes encoding them can lead to disruption of the entire system. The realization of cholesterol homeostasis largely depends on the amount and spectrum of steroids, as well as other lipids that make up food, the intensity of endogenous cholesterol synthesis, its absorption from the digestive tract, destruction and transformation into other compounds by tissue and microbial enzymes, the relationship with bile acids, the intensity of their intestinal-hepatic circulation, the amount of excretion with feces, hormonal status, and other factors. Healthy people receive about 0.5 g of animal cholesterol and similar plant sterols (phytosterols) daily with food. About 1.0 g of cholesterol is synthesized daily in the cells of the liver, intestines, ovaries, adrenal glands, kidneys and aorta [13,14]. In the liver, food and endogenous cholesterol (up to 1.0 g per day) is oxidized into bile acids; transport forms of cholesterol are also formed here. About 40 mg of cholesterol is consumed daily for the synthesis of steroid hormones [15,16].

Food and endogenous cholesterol in the intestine are partially reabsorbed in the form of chylomicrons, undergoing intestinal-hepatic recirculation. The rest of it (under normal conditions up to 500-800 mg per day), originating from food, bile, and the drained cellular intestinal epithelium, is excreted unchanged from the body (20-40%); in the form of microbial enzymes (60-80%) – coprostanol, coprostanon, cholestenone, stigmasterol, campesterol, beta-sitosterol, epicoprostanol, lanosterol, dehydrolanosterol, metosterol and further products of their degradation [17]. Dysbiosis is classified into 4 stages [18,19].

I – a decrease in the number of obligate representatives (bifidobacteria and /or lactobacilli) by 1-2 orders of magnitude, without an increase in the conditionally pathogenic microflora (CPM), an increase in the number of UPM with a normal number of bifidobacteria.

II – a moderate or significant decrease in the number of bifidobacteria, combined with pronounced changes in the aerobic microflora (reduction of lactobacilli, the appearance of altered forms of E. coli, UPM in high quantities).

III and IV – a large number of CPM both of one type and in associations, isolation of pathogenic microorganisms.

3 Material and Methods

During the retrospective study, the medical histories of 167 patients with chronic coronary heart disease were analyzed. The sample included women aged 47-55 years with a history of information about the presence of disorders from lipid metabolism and intestinal dysbiosis of varying degrees. Concomitant factors were the presence of grade I-II obesity in 74% of women with newly diagnosed hyperglycemia. For the analysis, the patients were divided into 4 groups:

The control group consisted of 50 women with a history of chronic coronary artery disease, dyslipidemia and atherosclerosis of the coronary arteries. At the same time, patients in this group had no information about the presence of dysbiosis.

The first group (I) consisted of 39 patients with chronic CHD, dyslipidemia, atherosclerosis and dysbiosis of I-II degree.

The second group (II) consisted of 34 patients with chronic CHD, dyslipidemia, atherosclerosis and dysbiosis of the III degree.

The third group (III) consisted of 44 patients with chronic CHD, dyslipidemia, atherosclerosis and dysbiosis of the IV degree.

To assess changes in lipid metabolism, the concentration of total cholesterol, high-density lipoprotein cholesterol, low lipoprotein cholesterol, and triglycerides were determined. The concentration of venous glucose and glycated hemoglobin were taken into account as concomitant studies [20-23].

Quantitative data were processed by descriptive statistics methods and presented as an average ± error of the average. All the correlation indicators discussed are statistically reliable ($p < 0.05$). The analysis was carried out using the MS Excel 2013 software package using parametric statistics methods by calculating the Student's criterion [24].

4 Results and Discussion

Among patients with chronic forms of coronary heart disease, lipid metabolism disorders were detected in all patients (Table 1).

Table 1: Indicators of lipid metabolism, glucose and glycated hemoglobin in women with chronic ischemic heart disease

Indicators	Control group	I	II	III
Total cholesterol	6.0±0.25	7.3±0.79	8.1±0.31**	8.8±0.27**
Thyroglobulin	1.2±0.43	1.2±0.57	1.6±0.39	2.2±0.15*
High-density lipoprotein cholesterol	1.2±0.36	1.2±0.28	1.1±0.49	1.1±0.44
Low-density lipoprotein cholesterol	4.1±0.23	5.2±0.63	5.3±0.31*	5.6±0.22**
Atherogenicity index	3.8±0.4	3.9±0.48	4.3±0.21	4.5±0.29
Glucose (venous)	5.8±0.48	6.2±0.31	6.1±0.58	6.1±0.53
Glycated hemoglobin	6.3±0.32	7.3±0.51	7.4±0.31	7.4±0.23*

* - $p \leq 0,05$ statistically reliable relative to the indicators in the control group

** - $p \leq 0,005$ high reliability relative to the indicators in the control group

The examined patients revealed a statistically significant increase in total cholesterol in groups II and III compared to the control group, which may be due to a decrease in the compensatory possibility of sterol regulation mechanisms in patients with grade III and IV dysbiosis due to the suppression of normal microbiota. Most likely, the violation of compensatory mechanisms affects the metabolism of exogenous cholesterol to a greater extent, which is confirmed by the absence of statistically significant changes in the indicators of the "liver panel" (Table 2).

Table 2: Indicators of the "liver panel"

	Control group	I	II	III
Total protein	19±0.59	19±0.72	20±0.41	20±0.57
Alanine aminotransferase	31±0.76	30±0.68	31±0.59	33±0.74
Aspartate aminotransferase	32±0.73	32±0.61	33±0.51	33±0.52
Gamma-glutamyltranspeptidase	31±0.54	31±0.55	31±0.58	32±0.73
Alkaline phosphatase	91±0.61	91±0.41	90±0.78	92±0.83

There is a statistically significant increase in triglycerides in group III compared to the control group, which is most likely due to a violation of triglyceride transport through the intestinal wall in patients with a high degree of dysbiosis.

The high reliability of an increase in the concentration of low-density lipoproteins may occur due to increased intake and synthesis of cholesterol and a decrease in compensatory mechanisms for regulating lipid metabolism.

A significant increase in glycated hemoglobin is observed only when comparing group III patients with controls, which may be associated with an increase in the toxic effects of metabolic products of opportunistic flora on the body.

5 Conclusion

Thus, in patients with coronary heart disease against the background of intestinal dysbiosis of III-IV degrees, significant lipid metabolism disorders associated with an increase in cholesterol,

low-density lipoproteins, and triglycerides are observed. Based on the data obtained on the absence of significant changes in liver tests, it can be concluded that the leading role of the exogenous lipid intake pathway is in the formation of dyslipidemia. Disorders of lipid metabolism in persons with dysbiosis can be observed due to the suppression of normal aerobic microflora by pathogenic microorganisms, which in turn can aggravate the manifestation of the underlying disease [25-27].

6 Availability of Data and Material

Data can be made available by contacting the corresponding author.

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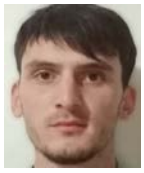

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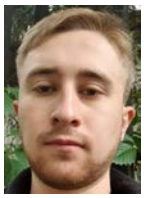

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