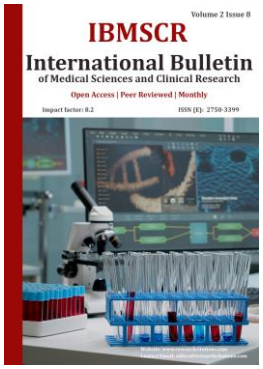

THE INFLUENCE OF CHANGES IN THE INTESTINAL MICROBIOTA ON DYSLIPIDEMIA IN PATIENTS WITH ISCHEMIC HEART DISEASE

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Abstract

Changes in the metabolism of the intestinal microbiome during the development of dyslipidemia, atherosclerosis and cardiovascular diseases have been studied in scientific research. Changes in the gut microbiome were studied for lipid metabolism, increased trimethylamine N oxide, short-chain peptides, and cholesterol homeostasis through the enterohepatic circulation. Probiotic use has been shown to increase Lactobacillus and Bifidobacterium species in the gut microbiota and decrease cholesterol, low-density lipoprotein, and triglycerides.

Key words: intestinal microbiota, microbiome, metabolism, lipid metabolism, dyslipidemia, atherosclerosis, probiotic

АННОТАЦИЯ

Изменения в метаболизме кишечного микробиома при развитии дислипидемии, атеросклероза и сердечно-сосудистых заболеваний были изучены в ходе последних научных исследований. Было изучено влияние изменений в микробиоме кишечника на липидный обмен, увеличение содержания триметиламина N оксида, короткоцепочечных пептидов на гомеостаз холестерин через энтерогепатическую циркуляцию. Было показано, что использование пробиотиков приводит к увеличению количества видов лактобактерий и бифидобактерий в кишечной микробиоте и снижению уровня холестерина, липопротеидов низкой плотности, и триглицеридов.

Ключевые слова: кишечная микробиота, микробиом, метаболизм, липидный обмен, дислипидемия, атеросклероз, пробиотик

Obesity is an important risk factor for the cardiovascular system and leads to the development of type 2 diabetes, hypertension and hyperlipidemia, as well as ischemic heart disease. [1, p. 175–189; 5, p. 632–642.]. In men and women, hypercholesterolemia is directly related to the prevalence of ischemic heart disease. [3, p. 5993–6006.]. Dietary modifications aimed at lowering blood cholesterol are the first line of treatment. However, patients' failure to properly follow the diet leads to an increase in the amount of lipoproteins in the body, which prevent the reduction of cholesterol, and even to an increase in the amount of low-density lipoproteins. The use of probiotics prevents cardiovascular disease and fights obesity. When systematic experiments were conducted, Lactobacillus and Bifidobacterium strains were commonly used as probiotics. [2, p. 228–242]. Potential probiotic mechanisms, hypocholesterolemic effect, active hydrolysis of bile salts, lowering of cholesterol using deconjugated bile acid salts, assimilation of bacterial cell membrane and transfer of cholesterol to conganprostanol by cholesterol enzyme reductase and SCFAs take place. [4, p. 36–49]. Dietary intervention affecting the intestinal microbiota is considered a new and cost-

effective method in the treatment of cardiometabolic diseases. According to research data, fermentable carbohydrates have a positive effect on the composition of the intestinal microbiota, while high amounts of animal fats and oils have a negative effect on the composition of the intestinal microbiota. Regular and adequate use of probiotics reduces cardiovascular risk factors. [5, p. 632–642].

The purpose of the study; development of preventive measures for assessment, treatment and prevention, taking into account that the change of intestinal microbiota affects the production of proatherogenic metabolite trimethylamine-N-oxide in patients with ischemic heart disease.

The object of the study; Research consists of clinical work. Clinical studies are conducted in 90 patients with ischemic heart disease. 30 of them were allocated to a healthy control group that did not suffer from ischemic heart disease.

Research subject; It consists of analyzing the results of clinical examination of patients treated in the therapeutic departments of the Andijan State Medical Institute, who are being treated for ischemic heart disease with angina pectoris. All of them were studied in the blood of short-chain peptides, trimethylamine N oxide, cholesterol, lipoproteins in low, very low and high density.

All biochemical changes in blood were studied in 4 groups (table 1).

1 - Table. Blood biochemical analysis results in 4 groups

Variables		**1-** group	**2-** group	**3-** group	**P**	**Total**
		(N=30)	(N=30)	(N=30)		(N=90)
The amount of cholecystokinin in the blood	Norm	3 (10.0%)	9 (30.0%)	2 (6.7%)	<0,001	14 (15.6%)
	patholog y	27 (90.0%)	21 (70.0%)	28 (93.3%)		76 (84,4%)
The amount of cholesterol in the blood	Norm	8 (26.7%)	15 (50.0%)	13 (43.3%)	<0.001	36 (40.0%)
	patholog y	21 (70.0%)	16 (53,3%)	17 (56.7%)		54 (60,0%)
The amount of triglycerides in the blood	patholog y	22 (73.3%)	28 (93.3%)	15 (50.0%)	<0.01	65 (72,2%)
	Norm	8 (26.7%)	2 (6.7%)	15 (50.0%)		25 (27,7%)
Low density lipoproteins	Norm	1 (3.3%)	5 (16.7%)	3 (10.0%)	<0.01	9 (8.3%)
	patholog y	29 (96.7%)	26 (86,7%)	26 (86,7%)		81 (90.0%)
High density lipoproteins	patholog y	2 (6,7%)	1 (3.3%)	1 (3,3%)	<0.001	27 (22.5%)
	Norm	28 (93,3%)	29 (96,7%)	29 (96,7%)		86 (95,5%)

As we can see in the above table, pathological indicators of CCK-8 were observed in all groups: 27 patients (90.0%) in group 1, 21 patients (70.0%) in group 2; In 28 patients (93.3%) in 3 groups, an increase in CCK-8 with increasing TMAO was observed (p<0.001); In total, 84.4% increase of CCK-8 was observed in 76 patients in all three groups.

When we look at triglyceride, in all three groups, respectively; 1 group - 21 (70.0%), 2 group - 16 patients (53.3%), 3 group - 17 patients (56.7%). An increase in triglycerides was observed in 54 patients with IHD by 60% (p<0.01).

When we looked at cholesterol, it was observed in 22 (73.3%) people in group 1, 28 (93.3%) in group 2, and 15 (50.0%) in group 3. In 65 patients with general IHD, an increase in cholesterol was observed by 72.2% (p<0.001).

Low-density lipoproteins and TMAO have been shown to increase together. 29 patients (96.7%) in group 1, 26 patients (86.7%) in group 2, 26 patients (86.7%) in group 3, and 90% increase in low-density lipoproteins was observed in 81 patients with IHD.

When we studied high-density lipoproteins, increased TMAO decreased high-density lipoproteins and reduced protection against atherosclerosis. 28 people in group 1 (93.3%), 29 people in group 2 (96.7%); It was observed in 29 people (96.7%) in 3 groups. Among 86 patients with IUD, 95.5% of patients had a decrease in high-density lipoproteins. (p<0.001).

When we see these indicators in the pictures, compared to the control group, the increase of CCK-8, cholesterol, triglyceride, and low-density lipoproteins was clearly demonstrated.

2 Table. Confidence levels of indicators

Variables		OR	95 CI		p
The amount of cholecystokinin in the blood	norm	Ref.			
	pathology	49,4	14,79	229,83	<0,001
The amount of cholesterol in the blood	norm	Ref.			
	pathology	0,27	0,1	0,66	0,006
The amount of triglycerides in the blood	norm	Ref.			
	pathology	0,40	0,11	1,16	0,118
Low density lipoproteins	norm	Ref.			
	pathology	0,30	0,02	1,71	0,266
High density lipoproteins	norm	546,0	79,85	1169,57	<0,001
	pathology	Ref.			
The amount of ALT in the blood	norm	Ref.			
	pathology	2,73	1,02	8,71	0,062
The amount of ALS in the blood	norm	Ref.			
	pathology	4,74	1,51	20,9	0,016

The changes in biochemical analysis of respondents' blood due to the increase in TMAO concentration were studied and the following results were obtained.

It was clinically proven that an excess of TMAO was associated with a 50-fold increase in the probability of a pathological increase in Cholecystokinin in blood [OR = 49.4], the confidence

interval calculated on the basis of Euler's constant and Fisher's r value also showed that the obtained results were statistically significant [CI 95% (14.79-229.83) p-value <0.001].

It was clinically proven that excess TMAO was associated with a 4-fold increase in blood cholesterol [OR = 0.27], the confidence interval calculated on the basis of Euler's constant and Fisher's r value also showed that the obtained results were statistically significant [CI 95% (0.1- 0.66) p-value =0.006].

A 2.5-fold increase in "Blood triglycerides" with excess TMAO was clinically relevant [OR = 0.40], and the confidence interval calculated based on Euler's constant and Fisher's r value showed that this effect was not statistically significant [CI 95% (0.11-1.16) p -value =0.118].

An excess of TMAO was found to reduce the odds of normal low-density lipoprotein by 70% [OR = 0.30], but the confidence interval calculated using Euler's constant and Fisher's r value showed that this effect was not statistically significant [CI 95 % (0.02-1.71) p-value =0.266].

It was clinically proven that excess TMAO was associated with a 546-fold increase in the probability of pathologically elevated high-density lipoprotein [OR = 546], the confidence interval calculated based on Euler's constant and Fisher's r value also showed that the obtained results were statistically significant [CI 95 % (79.85-1169.57) p-value <0.001].

It was clinically proven that excess TMAO was associated with a 2.73-fold increase in the probability of pathological elevation of ALT in the blood [OR = 2.73], although the confidence interval calculated based on Euler's constant showed this result to be statistically significant, but Fisher's r value was statistically significant. showed no significance [CI 95% (1.02-8.71) p-value =0.062].

It was clinically proven that an excess of TMAO was associated with a 4.74-fold increase in the probability of pathological elevation of blood AST [OR = 4.74], the confidence interval calculated based on Euler's constant and Fisher's r value showed that this result was statistically significant [CI 95% (1.51 -20.9) p-value =0.016]

In patients with IHD (stable tension angina FS 2.3) with an increase in trimethylamine-N-oxide, the parameters of the lipid spectrum were TG 72.2%, XS 58.2%, low-density lipoproteins increased by 83.5%, high-density lipoproteins increased by 69.2 % decrease was observed.

Lipid metabolism leads to the disturbance of intestinal microflora in the human body and the development of atherogenesis. Each person has an individual microbiota composition and has been shown to be involved in the development of dyslipidemia. The use of probiotics increases the number of lactobacilli and bifidumbacilli in the human body and plays a key role in preventing the development of atherosclerosis. In the future, the increase of such research will help in the development of new diagnostic protocols and treatment and preventive measures in cardiovascular diseases.

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