

The Influence of Food Patients on the Quantity of Trimethylamine-N Oxide in Patients with Ischemic Heart Disease

Kholikova Dilrabo Sobirjonovna^{*}, Jo'raeva Moxigul Azimjznovna

Andijan State Medical Institute, Andijan, Uzbekistan

Abstract During the study, 90 patients with ischemic heart disease and 30 controls without ischemic heart disease studied the effect of diet on the amount of trimethylamine. The effect of consumption of various products (eggs, beef, lamb, dairy products, cheese) on the increase in TMAO concentration was studied and relevant results were obtained. It has been clinically proven that the probability of pathologically increased TMAO concentration in individuals who consume "fish meat" products 3 or more times a week is 8 times lower than in those who consume 2 or less times a week.

Keywords Microbiota, Atherosclerosis, Ischemic heart disease, Nutrition, Choline metabolites, Trimethylamine-N-oxide TMAO

1. Introduction

Trimethylamine-N-oxide (TMAO), a choline metabolite, is associated with inflammation and is an active signaling metabolite in the gut microbiota leading to atherosclerotic damage and arterial thrombosis [2, p. 564–575]. When studying sterile rats, it was found that the microbiota affects the synthesis of endothelial adhesion molecules. [1, p. 691]. Red meat, egg yolks contain large amounts of L-carnitine and phosphatidylcholine. [9, p. 1585–1595; 3, p. 373–387]. This substance is converted into trimethylamine (TMA) by bacterial trimethylamine (TMA)-lyases in intestinal microbiota [1, p. 111–1; 800–804]. Such a reaction depends on the intestinal transport of choline and L-carnitine. When people eat food rich in choline, they may experience a fishy odor. Therefore, the formation of TMA depends on the dose of choline. In their research, when rats were given a low dose of choline (1.5 mmol/kg body weight), only 9 μ mol of choline (6% of the dose) reached the bacteria-rich gut. In rats, 237 μ mol (16% of the dose) reached the colon compared to 15 mmol choline/kg body weight. At both doses, 64–65% of administered choline was observed to be absorbed from the gut at 3 hours. [11, p. 111–1]. Therefore, TMA is converted to TMAO in the liver with the help of flavin-capturing monooxidase enzyme. [11, p. 111–1] Increased TMAO is also observed in insulin resistance, and elevated TMAO levels have been observed in diabetes. [6, p. 3699–3712]. In

addition, TMAO also affects the angiotensin II signal, which has a chronic effect on hypertension [8, p. 1700–1705] and affects vascular diseases and inflammation of the vessel wall. [7, p. 964–970; 8, p. 1317–1323]. The amount of L-carnitine in plasma was determined as a predictor of cardiovascular diseases, and dietary choline and TMAO supplementation were found to cause atherosclerosis in rats [4, p. 576–585; 9, p. 1585–1595]. However, in other studies, atherosclerotic changes were not observed in rats. [5, p. d2318–2326].

A separate questionnaire was distributed to all patients when we studied the level of increased TMAO in the study.

Human dietary preferences have been found to be linked to gut microbes. Rational nutrition, non-drug therapy is a type of prevention of the cardiovascular system. The BJST recommends that people eat less salt, less saturated fat and trans fat, and more fruits and vegetables.

In recent years, information on TMAO as an atherogenic metabolite has increased. Reducing the potential atherogenic metabolites of foods that lead to TMAO leads to a reduction in cardiovascular risk.

Intestinal microbiota is seen as a risk factor for the development of atherosclerosis and arterial thrombosis. Microbiota metabolites, trimethylamine N-oxide and short-chain fatty acids, are thought to stimulate and act as messengers of signaling mechanisms and cells of the immune system in the vascular system. In addition, microbiome-associated molecular patterns govern atherogenesis, and microbiota have been studied to induce arterial thrombosis through Toll-like receptor signaling. Increased atherogenic TMAO in patients with ischemic heart disease is associated with changes in gut microbiota and food intake.

^{*} Corresponding author:

d.abdullaevich@gmail.com (Kholikova Dilrabo Sobirjonovna)

Received: Nov. 4, 2023; Accepted: Nov. 24, 2023; Published: Dec. 16, 2023

Published online at <http://journal.sapub.org/ajmms>

2. Main Body

2.1. Purpose of the Study

Studying and evaluation of the effects of products consumed by patients with ischemic heart disease on the amount of trimethylamine.

2.2. Material and Methods of Research

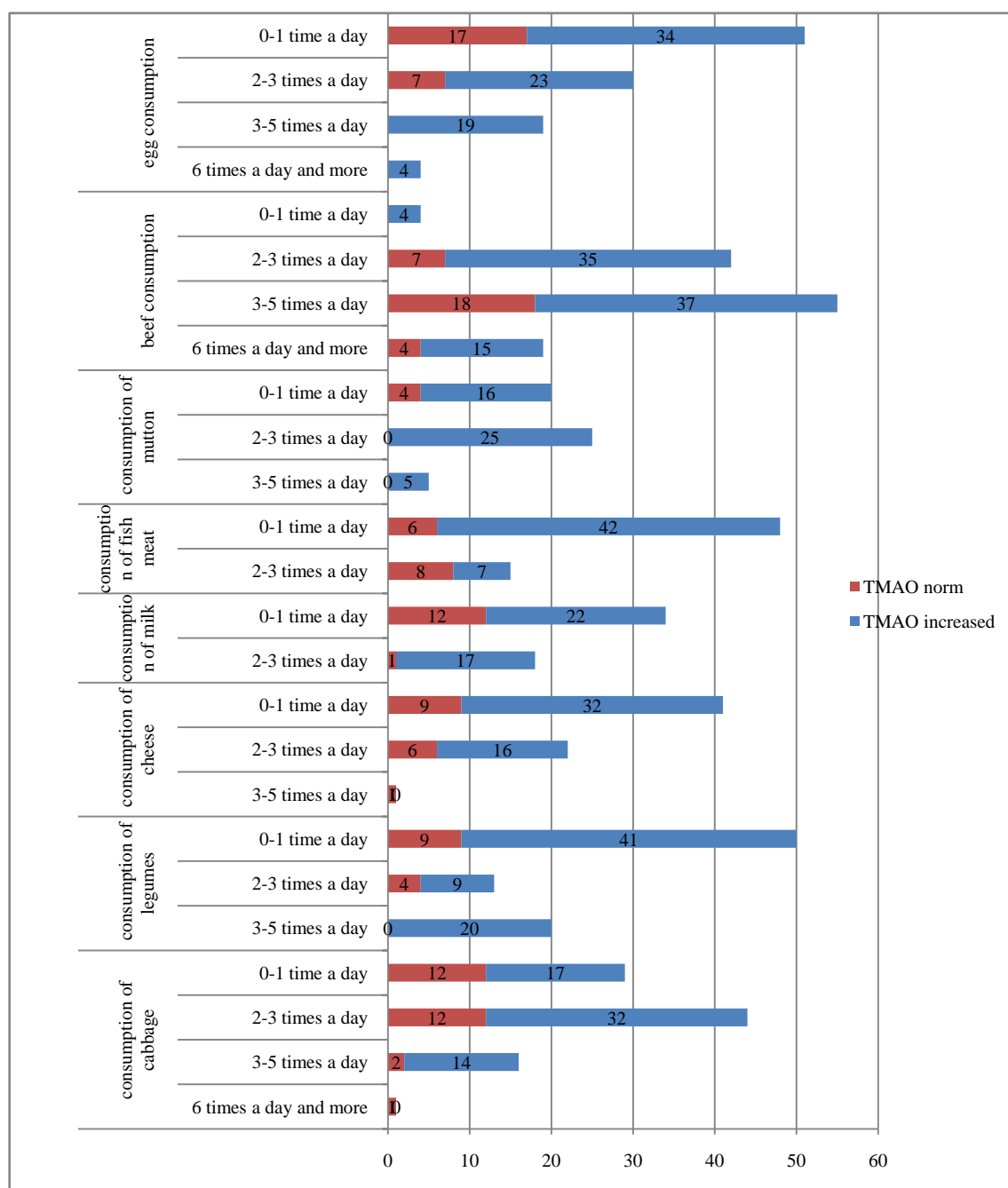
The research is conducted on 90 patients with ischemic heart disease and 30 healthy control group who did not suffer

from IHD and were treated in the therapeutic departments of the Andijan State Medical Institute.

Short chain peptides, trimethylamine N oxide, cholesterol, low, very low and high density lipoproteins were studied in the blood of all patient.

2.3. The Results Obtained and Their Discussion

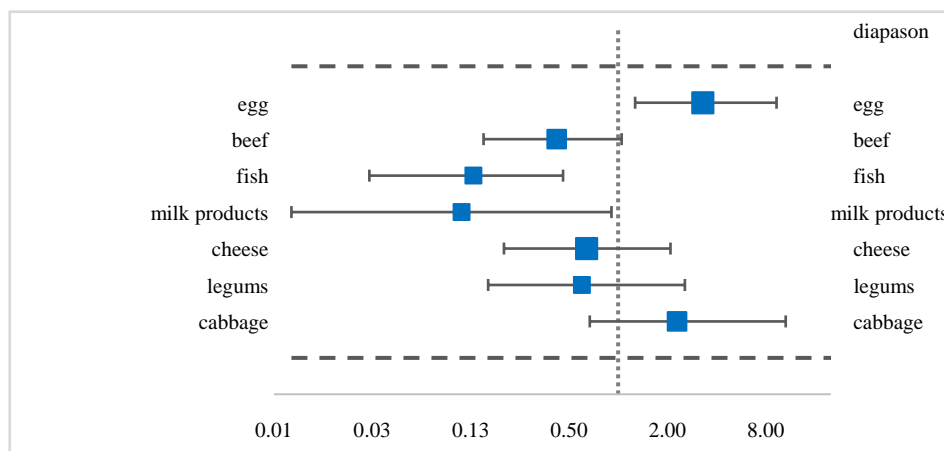
As we can see in the table, there was an increase in TMAO in recipients who consumed more than 3 times of all products, especially red meat and egg products.



Picture 1. Effect of consumed products on TMAO

Table 1. Effects of consumed products on TMAO

Variables		TMAO increased	TMAO norm	p	Total
		(N=90)	(N=30)		(N=120)
Consumption of eggs (within a week)	0-1 pcs	33 (36.7%)	17 (58.6%)	0.007	51 (42.1%)
	2-3 pcs	23 (25.3%)	7 (24.1%)		30 (24.8%)
	3-5 pcs	23 (25.3%)	0 (0%)		23 (19.0%)
Consumption of beef (within a week)	0-1 pcs	4 (4.4%)	0 (0%)	0.149	4 (3.3%)
	2-3 pcs	35 (38.9%)	7 (23.3%)		42 (34.7%)
	3-5 pcs	52 (57.8%)	22 (73.3%)		74 (61.2%)
Consumption of Mutton (within a week)	0-1 pcs	16 (17.8%)	4 (13.3%)	0.038	20 (16.5%)
	2-3 pcs	25 (27.8%)	0 (0%)		25 (20.7%)
	3-5 pcs	5 (5.6%)	0 (0%)		5 (4.1%)
Consumption of fish (within a week)	0-1 pcs	42 (46.7%)	6 (20.7%)	0.003	48 (39.7%)
	2-3 pcs	7 (7.8%)	8 (27.6%)		15 (12.4%)
drinking milk (within a week)	0-1 pcs	22 (24.4%)	12 (41.4%)	0.043	34 (28.1%)
	2-3 pcs	17 (18.9%)	1 (3.4%)		18 (14.9%)
Consumption of cheese (within a week)	0-1 pcs	32 (35.6%)	9 (31.0%)	0.196	41 (33.9%)
	2-3 pcs	16 (17.8%)	6 (20.7%)		22 (18.2%)
	3-5 pcs	0 (0%)	1 (3.4%)		1 (0.8%)
Consumption of legumes (within a week)	0-1 pcs	41 (45.6%)	9 (31.0%)	0.457	50 (41.3%)
	2-3 pcs	9 (10%)	4 (13.8%)		13 (10.7%)
	3-5 pcs	2 (2.2%)	0 (0%)		2 (1.7%)
Consumption of cabbage (within a week)	0-1 pcs	17 (18.9%)	12 (41.4%)	0.204	29 (24.0%)
	2-3 pcs	32 (35.6%)	12 (41.4%)		44 (36.4%)
	3-5 pcs	14 (15.6%)	3 (10.3%)		17 (14.0%)

**Picture 2.** Dietary reliability results

The effect of consumption of different products on the increase in TMAO concentration was studied and as a result: it was clinically proven that the probability of increasing the concentration of TMAO at a pathological level in individuals who consume the "Egg" product 2 or more times a week is 3.29 times higher than in those who consume it 1 or less times a week [OR = 3.29], 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% (1.27-9.32) p-value = 0.018].

It was clinically proven that the probability of pathologically increased TMAO concentration in individuals consuming "Beef" product 4 or more times a week is 2.5

times lower than those consuming 3 or less times a week [OR = 0.42], but, the confidence interval calculated on the basis of Euler's constant and Fisher's The r value showed that the obtained results were not statistically significant [CI 95% (0.15-1.05) p-value = 0.076].

It was clinically proven that individuals consuming 3 or more fish products per week had a 8-fold lower probability of pathological increase in TMAO concentration than those consuming 2 or less products per week [OR = 0.13], 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% (0.03-0.46) p-value = 0.002].

Table 2. Determining the reliability of consumed products

Variables		OR	95 CI		p
Consumption of eggs (within a week)	1 and less	Ref.			
	2 and more	3,29	1,27	9,32	0,018
Consumption of beef (within a week)	2-3 times	Ref.			
	3-5 times	0,42	0,15	1,05	0,076
Consumption of fish (within a week)	2-3 times	Ref.			
	3-5 times	0,13	0,03	0,46	0,002
Drinking milk (within a week)	0-1 times	Ref.			
	2-3 times	0,11	0,01	0,91	0,018
Consumption of cheese (within a week)	2-3 times	Ref.			
	3-5 times	0,64	0,2	2,09	0,454
Consumption of legumes (within a week)	2-3 times	Ref.			
	3-5 times	0,60	0,16	2,56	0,465
Consumption of cabbage (within a week)	2-3 times	Ref.			
	3-5 times	2,29	0,67	10,6	0,226

It was clinically proven that the probability of pathologically increased TMAO concentration in individuals who consume milk products 2-3 times a week is 9 times lower than those who consume it 0-1 times a week [OR = 0.11], the confidence interval calculated on the basis of Euler's constant and Fisher's r value were also obtained the results showed statistical significance [CI 95% (0.01-0.91) p-value = 0.0018].

It was clinically proven that the probability of pathologically increased TMAO concentration in individuals who consume "cheese" product 2 or less times a week is 36% lower than those who consume it 3 or less times a week [OR = 0.64], but the confidence interval calculated based on Euler's constant and Fisher's r value also showed that the obtained results were not statistically significant [CI 95% (0.2-2.09) p-value = 0.454].

3. Conclusions

Compared to the control group, the consumption of products rich in phosphatidylcholine and L-carnitine in the diet of patients with IHD was 6 times greater than that of the control group: meat ($r < 0.05$), beef ($r < 0.05$), dairy products ($r < 0.05$), eggs 3 and higher times observed.

REFERENCES

- [1] Anna Lässiger-Herfurth; Giulia Pontarollo; Alexandra Grill; Christoph Reinhardt; / The Gut Microbiota in Cardiovascular Disease and Arterial Thrombosis // *Microorganisms* 2019, 7(12), 691.
- [2] Ascher, S.; Reinhardt, C. The gut microbiota: An emerging risk factor for cardiovascular and cerebrovascular disease. *Eur. J. Immunol.* 2018, 48, 564–575.
- [3] Koeth, R.A.; Lam-Galvez, B.R.; Kirsop, J.; Wang, Z.; Levison, B.S.; Gu, X.; Copeland, M.F.; Bartlett, D.; Cody, D.B.; Dai, H.J.; et al. L-Carnitine in omnivorous diets induces an atherogenic gut microbial pathway in humans. *J. Clin. Investig.* 2019, 129, 373–387.
- [4] Koeth, R.A.; Wang, Z.; Levison, B.S.; Buffa, J.A.; Org, E.; Sheehy, B.T.; Britt, E.B.; Fu, X.; Wu, Y.; Li, L.; et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nat. Med.* 2013, 19, 576–585.
- [5] Lindskog Jonsson, A.; Caesar, R.; Akrami, R.; Reinhardt, C.; Fåkk Hållenius, F.; Borén, J.; Bäckhed, F. Impact of gut microbiota and diet on the development of atherosclerosis in Apoe^{-/-} mice. *Arterioscler. Thromb. Vasc. Biol.* 2018, 38, 2318–2326.
- [6] Oellgaard, J.; Winther, S.A.; Hansen, T.S.; Rossing, P.; von Scholten, B.J. Trimethylamine N-oxide (TMAO) as a new potential therapeutic target for insulin resistance and cancer. *Curr. Pharm. Des.* 2017, 23, 3699–3712.
- [7] Sun, G.; Yin, Z.; Liu, N.; Bian, X.; Yu, R.; Su, X.; Zhang, B.; Wang, Y. Gut microbial metabolite TMAO contributes to renal dysfunction in a mouse model of diet-induced obesity. *Biochem. Biophys. Res. Commun.* 2017, 493, 964–970.
- [8] Ufnal, M.; Jazwiec, R.; Dadlez, M.; Drapala, A.; Sikora, M.; Skrzypecki, J. Trimethylamine-N-oxide: A carnitine-derived metabolite that prolongs the hypertensive effect of angiotensin II in rats. *Can. J. Cardiol.* 2014, 30, 1700–1705.
- [9] Wang, Z.; Roberts, A.B.; Buffa, J.A.; Levison, B.S.; Zhu, W.; Org, E.; Gu, X.; Huang, Y.; Zamanian-Daryoush, M.; Culley, M.K.; et al. Non-lethal inhibition of gut microbial trimethylamine production for the treatment of atherosclerosis. *Cell* 2015, 163, 1585–1595.
- [10] Zeisel, S.H.; daCosta, K.A.; Youssef, M.; Hensey, S. Conversion of dietary choline to trimethylamine and dimethylamine in rats: Dose-response relationship. *J. Nutr.* 1989, 119, 800–804.
- [11] Zhu, W.; Gregory, J.C.; Org, E.; Buffa, J.A.; Gupta, N.; Wang, Z.; Li, L.; Fu, X.; Wu, Y.; Mehrabian, M.; et al. Gut microbial metabolite TMAO enhances platelet hyperreactivity and thrombosis risk. *Cell* 2016, 165, 111–1.
- [12] Zhu, W.; Gregory, J.C.; Org, E.; Buffa, J.A.; Gupta, N.; Wang, Z.; Li, L.; Fu, X.; Wu, Y.; Mehrabian, M.; et al. Gut microbial metabolite TMAO enhances platelet hyperreactivity and thrombosis risk. *Cell* 2016, 165, 111–1.