ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

Therapy

UDC: 616.12-008.313.2

INFLUENCE OF THE LONG-TERM POSTBIOTICS PRESCRIPTION ON CARDIOMETABOLIC RISK FACTORS IN PATIENTS WITH CORONARY ARTERY DISEASE AND ATRIAL FIBRILLATION

Melnychuk I.O., Kramarova V.N.
Bogomolets National Medical University, Kyiv, Ukraine

The aim of this research was to evaluate the influence of long-term postbiotics prescription on CardioMetabolic Risk Factors (CMRF) in patients with Coronary Artery Disease (CAD) and Atrial Fibrillation (AF). 124 patients with CAD and AF paroxysm patients were divided by stratified randomization 1:3 into two groups: I (31 patients) and II (93 patients). Stratification was done according to the patient's age, gender, body mass index, and Total Cholesterol (TC). All patients received Standard Therapy (ST), according to the latest European Society of Cardiology guidelines: β-blockers, HMG-CoA-inhibitors (statins), anticoagulants, and, if necessary, angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers, calcium antagonists, diuretics, and/or antiarrhythmics. The I group patients' received ST and postbiotic prescription during 6 months: rebamipide (2-(4-chlorobenzolamino)-3-[2(1H))-quinolon-4-yl] propionic acid) (100 mg 3 times a day) and glycine (100 mg 3 times a day). The II group patients received only ST. All patients were examined two times: during the initial investigation and after 6 months of treatment. After treatment in I group patients' a significant decrease in TC (by 10.00%), low density lipoproteins (by 19.50%), Apolipoprotein B (by 12.92%), Interleucin-6 (by 12.40%), C-reactive protein (by 15.89%), TriMethylAmine (TMA) (by 19.32%), TriMethylAmine-N-Oxide (TMAO) (by 27.24%) was found ($p<0.05$) versus II group patients. After treatment all patients had significant improvement in CMRF ($p<0.05$): TC (by 44.01%), low density lipoproteins (by 52.90%), Interleucin-6 (by 27.52%), C-reactive protein (by 20.13%), TMA (by 14.66%), TMAO (by 33.91%), and significant increase in TMA/TMAO (by 23.45%), but I group got better values. In conclusion, long-term (6 months) postbiotics (propionic acid and glycine) prescription has a marked positive influence on CMRF in patients with CAD and AF.

Keywords: *glycine, propionic acid, arrhythmia, cardiovascular disorders, dyslipidemia, inflammation.*

Цитуйте українською: Мельничук ІО, Крамарова ВН. Вплив довготривалого призначення постбіотиків на кардіометаболічні фактори ризику у пацієнтів з ішемічною хворобою серця та миготливою аритмією. Медицина сьогодні і завтра. 2024;93(2):11с. In press. https://doi.org/10.35339/msz.2024.93.2.mkr [англійською].

Cite in English: Melnychuk IO, Kramarova VN. Influence of the long-term postbiotics prescription on cardiometabolic risk factors in patients with coronary artery disease and atrial fibrillation. Medicine Today and Tomorrow. 2024;93(2):11p. In press. https://doi.org/10.35339/msz.2024.93.2.mkr

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

Відповідальний автор: Мельничук І.О.
✉ Україна, 01601, м. Київ,
бул. Тараса Шевченка, 13.
E-mail: ira.merkulova45@gmail.com

Corresponding author: Melnychuk I.O.
✉ Ukraine, 01601, Kyiv,
Tarasa Shevchenko Blvd, 13.
E-mail: ira.merkulova45@gmail.com

Introduction

Atrial Fibrillation (AF) and Coronary Artery Disease (CAD) are two highly prevalent cardiovascular disorders, which are associated with substantial mortality and morbidity. CAD and AF share a multiplicity of risk factors, such as obesity, arterial hypertension, dyslipidemia, inflammatory diseases, etc. Moreover, CAD by itself is a known AF risk factor. Near half of AF paroxysms occurred in CAD patients. The presence of CAD and AF aggravates the course of the disease and its prognosis [1; 2]. CardioMetabolic Risk Factors (CMRFs) encompass a broad spectrum of interrelated risk factors that are associated with a lifelong risk for CardioVascular Diseases (CVDs). Nowadays, a variety of CMRFs exist. Impaired glucose metabolism, dyslipidemia, and proinflammatory molecules are the most widely known [3].

Gut microbiota composition plays a crucial role in human health and disease. It influences the host's health through intestinal epithelial barrier dysregulation, which leads to endotoxemia and amplifies systemic inflammation. Also, gut microbiota metabolites are not the least important. High-circulated levels of TriMethylAmine (TMA) or TriMethylAmine-N-Oxide (TMAO) are directly connected with CVDs [4]. In animal studies, TMAO injection promotes arrhythmia, possibly by an increase in inflammatory cytokines expression. Also, increased TMAO levels are strongly correlated with thromboembolic events. Moreover, it is associated with a majority of known CMRFs – Body Mass Index (BMI), Total Cholesterol (TC), Low-Density Lipoproteins (LDL), systolic blood pressure, glucose level, smoking status, etc. [5; 6]. So, TMA, TMAO, and their ratio are undoubtedly part of CMRFs.

Postbiotics are defined as "non-viable bacterial products or metabolic products from microorganisms that have biological activity in the host". These include secreted Short-Chain Fatty Acids (SCFAs), Amino Acids (AAs), organic acids, biosurfactants and proteins, bacteriocins, vitamins, and peptides [7]. SCFAs are mostly represented by acetate, propionate, and butyrate. Propionate reduces renin release, which decreases blood pressure, and stimulates glucagon-like peptide-1 and peptide YY release obesity risk, which decreases obesity risks [5]. AAs are also promising postbiotics examples. They restore gut homeostasis through rebuilding the gut's epithelial cells microvilli, which procure intestinal integrity [8; 9]. Gut mucosa production closely depends on glycine, serine, and threonine exchange. Moreover, glycine has proven hepatoprotective, neuroprotective, anti-inflammatory, glucose, and lipids lowering properties [10; 11].

So, the role of gut microbiota in CVDs pathogenesis is apparent, such as the importance of searching for its correction ways.

The aim of study was to evaluate the influence of long-term (6 months) postbiotics (propionic acid and glycine) prescription on cardiometabolic risk factors in patients with coronary artery disease and atrial fibrillation.

Materials and Methods

A randomized trial was performed to correct the detected metabolic violations. Postbiotics were prescribed additionally. 124 patients with CAD and AF paroxysm patients were divided by stratified rando-

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

mization 1:3 into two groups: I (31 patients) and II (93 patients). Stratification was done according to the patient's age, gender, BMI, and TC. All patients received Standard Therapy (ST), according to the latest European Society of Cardiology guidelines: β-blockers, HMG-CoA-inhibitors (statins), anticoagulants, angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers (if necessary), calcium antagonists (if necessary), diuretics (if necessary), and antiarrhythmics (if necessary) [1; 2]. The I group patients received ST and postbiotic prescription [7]: rebamipide (2-(4-chlorobenzoylamino)-3-[2(1H))-quinolon-4-yl] propionic acid) by 100 mg 3 times a day and glycine by 100 mg 3 times a day during 6 months. At the same time, the II group patients received only ST. All patients were examined two times: during the initial investigation and after 6 months of treatment. The CMRFs changes in investigated patients during treatment are reported in this article. The study design is shown in *Fig.*

All patients were treated in the Kyiv City Clinical Hospital No.12 in cardiological and therapeutic departments in 2018–2023. Diagnosis CAD was confirmed by a history of coronary artery stenotic changes during invasive coronarography. AF paroxysm was checked by resting 12 leads electrocardiography. Exclusion criteria were: reported malignancies, chronic kidney disease (Glomerular Filtration Rate, GFR <60 mL/min), valvular AF, heart failure Class III to IV (by New York Heart Association) [2], thyroid pathology, inflammatory bowel disease, irritable bowel syndrome, vegetarians and vegans, pregnancy, taking probiotics and antibiotics for a month before the study.

Baseline characteristics of study patients include age, gender, history of myocardial infarction (MI), stroke, diabetes mellitus, obesity, BMI, uric acid, total bilirubin, GFR levels, and coagulation tests: Prothrombin Index (PI), Hematocrit (Ht), activated Partial Thromboplastin Time (aPTT), fibrinogen, fibrin. Uric acid, total bilirubin,

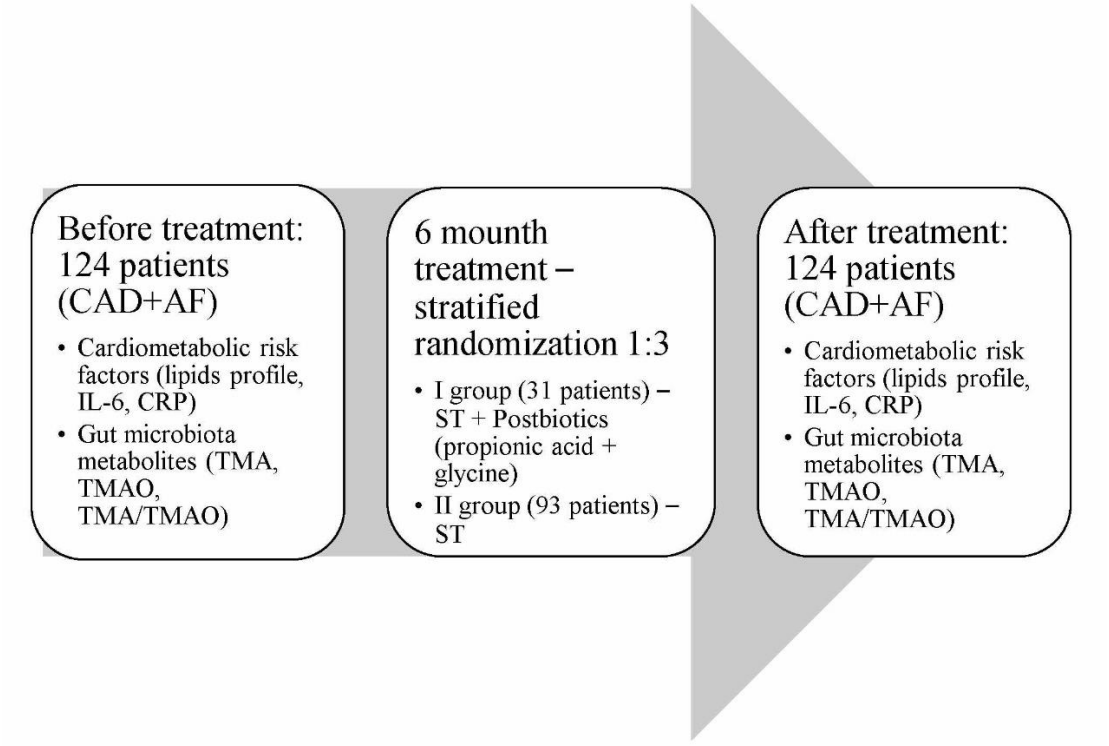

Fig. Study design.

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

creatinine, and coagulation tests were checked by the Kyiv City Clinical Hospital No.12 laboratory. Advanced age, obesity, prothrombotic state, high stages of chronic kidney disease, gout, and hyperbilirubinemia are known risk factors of AF paroxysm development [1]. That's why these baseline characteristics were analyzed and compared because it can help us to exclude their influence on obtained results.

We investigated such cardiometabolic risk factors: lipids indexes – TC, TriGlycerides (TG), LDL, High-Density Lipoproteins (HDL), Lipoprotein α (Lpα), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB); proinflammatory markers – C-Reactive Protein (CRP), InterLeukin-6 (IL-6); gut microbiota metabolites – TMA, TMAO, and SCFAs. Also, ApoB/ApoA1 and TMA/TMAO ratios were checked. Hymalyzer 2000 (reagent produced by HUMAN GmbH, Germany) was used for the detection of TC, TG, HDL, LDL (reagent produced by HUMAN GmbH, Germany), ApoA1, ApoB, Lpα, and CRP (reagent produced by Dialab, Austria) – by flow cytometry. Hymareader 2106 (ELISA) was used for the detection of IL-6 – reagents produced by Vector Best. The level of TMAO and TMA plasma was determined by gas chromatography with mass electron detection. They were extracted from blood plasma into acid by adding internal standards. The patient's blood sampling was performed on an empty stomach from the cubital vein on the day of hospitalization.

The study was conducted at the base and was approved by the ethical commission of the Kyiv City Clinical Hospital No.12 (protocol No.8 on August 22, 2018). Informed consent was obtained from all subjects by the Declaration of Helsinki.

Results were presented as a number for categorical variables. Variables distribution for normality were checked by the Pearson criterion. Data were compared using the Wilcoxon signed-rank test or Student t-test with two critical regions by the type of distribution [12]. All calculations were done in MATLAB R2014a (MathWorks, USA).

Results

At first, the baseline characteristics of the investigated groups were analyzed. Treated groups have no significant difference. The data are shown in *Table 1*.

After 6-mounth treatment period levels of CMRFs were compared in investigated groups. In the I group patients the significantly lower levels of TC (by 10.00%), LDL (by 19.50%), Apo B (by 12.92%), IL-6 (by 12.40%), CRP (by 15.89%), TMA (by 19.32%), TMAO (by 27.24%) in comparison with II group, $p<0.05$. All data are shown in *Table 2*.

Also, the dynamic of CMRFs changes in I group during 6 months was analyzed. After treatment in I group patients a significant decrease in TC (by 49.19%), LDL (by 62.66%), Apo B (by 13.24 %), Apo B/Apo A1 (by 9.66 %), IL-6 (by 31.84%), CRP (by 19.63%), TMA (by 22.90%), TMAO (by 43.31%), and an increase in TMA/TMAO (by 25.89%) was found versus before treatment results, $p<0.05$. All data are shown in *Table 3*.

Moreover, the dynamic of CMRFs changes in II group during 6 months was analyzed. After treatment in II group patients a significant decrease in TC (by 38.82%), LDL (by 39.93%), IL-6 (by 19.87%), CRP (by 12.54%), TMAO (by 23.21) in comparison with before treatment results, $p<0.05$. All data are shown in *Table 4*.

At least, the summarizing dynamic in CMRFs changes were analyzed. After treatment in investigated patients the significant decrease in TC (by 44.01%), LDL (by 52.90%), IL-6 (by 27.52%), CRP (by 20.13%), TMA (by 14.66%), TMAO (by 33.91%), and significant increase in TMA/TMAO (by 23.45%) was found, $p<0.05$. All data are shown in *Table 5*.

So, after treatment all patients had the significant positive dynamic in CMRFs

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

Table 1. Baseline characteristics of the treated groups (p>0.05)

Group Characteristic (measurement)	I	II
Age (years) *	69.61±2.01	67.61±1.07
Men (%)	48.39	47.31
History of myocardial infarction (%)	7.23	9.68
History of stroke (%)	7.23	9.68
Diabetes mellitus (%)	16.13	16.13
Obesity (%)	19.35	9.68
Smoking (%)	25.81	35.48
Uric acid (mmol/l) *	369.70±31.99	408.60±37.43
Total bilirubin (mmol/l) *	11.51±1.0	12.10±0.72
GFR (ml/min) *	64.52±6.83	60.96±2.19
BMI (kg/m^2) *	27.97±0.87	26.60±0.48
PI (%) *	76.95±0.78	77.40±1.54
Ht (%) *	46.47±1.29	44.91±0.74
aPTT (s) *	29.90±0.69	30.73±1.09
Fibrinogen (mg/dl) *	3.09±0.11	3.34±0.14
Fibrin (mg) *	15.73±0.77	14.93±0.78

Notes: * – (mean ± standard error), BMI – body mass index, GFR – glomerular filtration rate, PI – prothrombin index, Ht – hematocrit, aPTT – activated partial thromboplastin time, p – probability.

Table 2. The dynamic of CMRFs changes in I and II group patients after 6 months of treatment (p>0.05)

Characteristic	I group after treatment	II group after treatment
TC (mmol/l) *	3.70±0.10	4.07±0.14
TG (mmol/l) *	1.69±0.08	1.68±0.08
HDL (mmol/l) *	1.96±0.11	1.77±0.09
LDL (mmol/l) *	2.41±0.11	2.88±0.13
Apo A1 (g/l) *	1.60±0.09	1.47±0.08
Apo B (g/l) *	2.36±0.13	2.71±0.19
ApoB/ApoA1 *	1.59±0.12	1.96±0.22
Lpα (mg/dl) *	22.46±1.07	21.22±1.38
IL-6 (pg/ml) *	2.12±0.12	2.42±0.12
CRP (mg/l) *	2.17±0.06	2.58±0.17
TMAO (mmol/l) *	19.29±0.46	23.91±0.65
TMA (mmol/l) *	1.95±0.15	2.68±0.11
TMAO/TMA *	10.26±0.55	9.17±0.33

Notes: * – (mean ± standard error), TC – total cholesterol, TG – triglycerides, HDL – high-density lipoproteins, LDL – low-density lipoproteins, Apo A1 – apolipoprotein A1, Apo B – apolipoprotein B, Lpα – lipoprotein α, IL-6 – interleukin-6, CRP – C-reactive protein, TMAO – trimethylamine-N-oxide, TMA – trimethylamine, p – probability.

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

Table 3. The dynamic of CMRFs changes in I group patients after 6 months of treatment (p>0.05)

Characteristic	Before treatment	After treatment
TC (mmol/l) *	5.52±0.26	3.70±0.10
TG (mmol/l) *	1.86±0.17	1.69±0.08
HDL (mmol/l) *	1.77±0.17	1.96±0.11
LDL (mmol/l) *	3.92±0.39	2.41±0.11
Apo A1 (g/l) *	1.72±0.14	1.60±0.09
Apo B (g/l) *	2.92±0.20	2.36±0.13
ApoB/ApoA1 *	1.76±0.23	1.59±0.12
Lpα (mg/dl) *	26.12±2.05	22.46±1.07
IL-6 (pg/ml) *	3.31±0.24	2.12±0.12
CRP (mg/l) *	2.89±0.23	2.17±0.06
TMAO (mmol/l) *	25.02±1.17	19.29±0.46
TMA (mmol/l) *	3.44±0.47	1.95±0.15
TMAO/TMA *	8.15±0.94	10.26±0.55

Notes: * – (mean ± standard error), TC – total cholesterol, TG – triglycerides, HDL – high-density lipoproteins, LDL – low-density lipoproteins, Apo A1 – apolipoprotein A1, Apo B – apolipoprotein B, Lpα – lipoprotein α, IL-6 – interleukin-6, CRP – C-reactive protein, TMAO – trimethylamine-N-oxide, TMA – trimethylamine, p – probability.

Table 4. The dynamic of CMRFs changes in II group patients after 6 months of treatment (p>0.05)

Characteristic	Before treatment	After treatment
TC (mmol/l) *	5.65±0.15	4.07±0.14
TG (mmol/l) *	1.81±0.12	1.68±0.08
HDL (mmol/l) *	1.56±0.12	1.77±0.09
LDL (mmol/l) *	4.03±0.29	2.88±0.13
Apo A1 (g/l) *	1.59±0.12	1.47±0.08
Apo B (g/l) *	2.88±0.18	2.71±0.19
ApoB/ApoA1 *	2.07±0.28	1.96±0.22
Lpα (mg/dl) *	23.05±2.04	21.22±1.38
IL-6 (pg/ml) *	3.22±0.22	2.42±0.12
CRP (mg/l) *	3.05±0.32	2.58±0.17
TMAO (mmol/l) *	24.85±0.58	23.91±0.65
TMA (mmol/l) *	3.49±0.21	2.68±0.11
TMAO/TMA *	8.37±0.40	9.17±0.33

Notes: * – (mean ± standard error), TC – total cholesterol, TG – triglycerides, HDL – high-density lipoproteins, LDL – low-density lipoproteins, Apo A1 – apolipoprotein A1, Apo B – apolipoprotein B, Lpα – lipoprotein α, IL-6 – interleukin-6, CRP – C-reactive protein, TMAO – trimethylamine-N-oxide, TMA – trimethylamine, p – probability.

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

Table 5. The dynamic of CMRFs changes in all patients after 6 months of treatment (p>0.05)

Characteristic	Before treatment	After treatment
TC (mmol/l) *	5.53±0.13	3.84±0.15
TG (mmol/l) *	1.83±0.10	1.68±0.06
HDL (mmol/l) *	1.63±0.10	1.86±0.07
LDL (mmol/l) *	3.96±0.23	2.59±0.09
Apo A1 (g/l) *	1.65±0.09	1.54±0.06
Apo B (g/l) *	2.91±0.13	2.59±0.12
ApoB/ApoA1 *	2.00±0.19	1.78±0.03
Lpα (mg/dl) *	24.48±1.45	21.84±0.86
IL-6 (pg/ml) *	3.27±0.16	2.37±0.08
CRP (mg/l) *	3.03±0.19	2.42±0.09
TMAO (mmol/l) *	24.89±0.52	21.24±0.52
TMA (mmol/l) *	3.48±0.19	2.30±0.10
TMAO/TMA *	7.72±0.38	9.53±0.30

Notes: * – (mean ± standard error), TC – total cholesterol, TG – triglycerides, HDL – high-density lipoproteins, LDL – low-density lipoproteins, Apo A1 – apolipoprotein A1, Apo B – apolipoprotein B, Lpα – lipoprotein α, IL-6 – interleukin-6, CRP – C-reactive protein, TMAO – trimethylamine-N-oxide, TMA – trimethylamine, p – probability.

(decrease in proatherogenic and proinflammatory indexes), but in the I group, who obtained postbiotics supplementation such changes were noticeable.

Discussion

By the obtained results, long-term postbiotics additional prescription in patients with CAD and AF had a significant positive influence in CMRFs changes. Significant ($p<0.05$) decrease in TC (by 10.00%), LDL (by 19.50%), Apo B (by 12.92%), IL-6 (by 12.40%), CRP (by 15.89%), TMA (by 19.32%), TMAO (by 27.24%) was checked in patients who obtained additional long-term postbiotics prescription in comparison with ST therapy group. Postbiotics which were used include glycine and propionic acid.

Glycine is an aliphatic carboxylic amino acid with the lowest molecular weight. Due to its chemical structure, it is both hydrophilic and hydrophobic. According to some data, glycine is a relatively indispensable amino acid, because its synthesis in vivo is not always able to meet the metabolic needs of the body. The daily need for exogenous glycine is from 1.5 to 3 grams. Glycine makes up 11.5% of all amino acids in the human body and contains 20.0% of the nitrogen of protein amino acids. It is known that chronic glycine deficiency leads to various, mainly metabolic, diseases: type 2 diabetes, obesity, steatohepatosis, immunodeficiency, delayed physical and mental development in children [13].

It is difficult to exaggerate the metabolic value of glycine. Glycine is a proteinogenic amino acid, takes part in the regulation of gene expression, determines the configuration of proteins and their activity (including insulin), ensures the synthesis of glutathione, nitric oxide, etc. 80.0% of all glycine is used by the human body for protein synthesis. Synthesis of DNA, RNA, serine, creatine, heme is impossible without glycine. It was found that glycine has antioxidant properties, normalizes cholesterol metabolism in the liver, has endothelium-pro-

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

tective and anti-ischemic effects, significantly affects the exchange of divalent ions, catalyzes the exchange of non-esterified fatty acids. For example, in an animal model of myocardial infarction, glycine infusion into coronary arteries reduced the area of necrosis and accelerated metabolic and functional recovery [14; 15].

According to literature data, about 30% of glycine supplied with food is metabolized by the microbiota of the small intestine, and by both gram-positive and gram-negative flora. However, what determines the activity of glycine degradation by the intestinal microbiota is still unknown. For example, the activity of glycine degradation increases in patients with type 2 diabetes. It was found that patients who took probiotics (bifido and lactobacilli) had a lower concentration of glycine in their feces. An increase in the content of formic acid in the stool is a sign of increased glycine degradation under the influence of the gut microbiome. On the other hand, the state of the gut microbiome can influence the metabolism of glycine in the host's body due to changes in the expression of enzymes. It was found that intestinal dysbiosis has an effect on the development of NASH due to a decrease in the content of circulating glycine. Also, obesity and metabolic syndrome are closely associated with a decrease in circulating glycine and disruption of the gut microbiome [16].

The dose-dependent effect of glycine has long been known. However, taking glycine even in a dose of 85.0 g/day is not capable of causing side effects, which is explained by the ability of muscles, including cardiac muscles, to act as a glycine depot. When taking high doses of glycine from 15.0 g/day to 40.0 g/day, its excretion by the kidneys increases by only 5–10%, and the level in the blood plasma is doubled. Only an increase in the serum glycine level of more than 10,000 mmol/L can cause an increase in the blood ammonium level and toxic manifestations, namely dizziness, nausea, and vomiting [17]. It was found that the intake of glycine by healthy patients in high doses (0.8 g/kg/day) is capable of reducing negativism and increasing psychological resilience [18]. According to some data, taking glycine in a dose of 7.0 g/day is able to improve the state of the intestinal microbiome, namely to change the content of some types of Bifido- and Lactobacteria. There is also controversy regarding the ability of glycine to reduce the level of IL-6 and TNF-α in plasma, fecal IgA [19].

Propionic acid is a one of SCFAs, which are the important products of the dietary fiber gut microbiota fermentation. Propionate is also characterized by anti-inflammatory and anti-apoptotic properties, but in addition has anti-hypertensive and anti-lipidemic effects. Also, propionate is one of the products of tryptophan degradation by gut microbiota. Decrease of cardiac and circulating propionic acids levels is directly associated with heart failure development. In the animal experiments, propionic acids supplementation significantly improved the diastolic function and metabolic alterations by restoring NAD+ salvage pathways. On the other hand, the liver dysfunction leads for steatohepatitis formation, which connected with lipids metabolism alterations and associated with gut dysbiosis [20].

So, glycine and propionic acid are the crucial metabolites for myocardium and their supplementation is very perspective for further primary and secondary CVDs prophylaxis.

Conclusions

Long-term (6 months) postbiotics (propionic acid and glycine) prescription has a marked positive influence on cardiometabolic risk factors in patients with coronary artery disease and atrial fibrillation:

1. after treatment in patients who obtained long-term postbiotics additional prescription a significant decrease in TC (by 10.00%, $p<0.05$), LDL (by 19.50%, $p<0.05$), Apo B

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

(by 12.92%, p<0.05), IL-6 (by 12.40%, p< <0.05), CRP (by 15.89%, p< <0.05), TMA (by 19.32%, p<0.05), TMAO (by 27.24%, p<0.05) was found in comparison with patient who got only standard therapy;

2. after treatment all patients had significant improvement in cardiometabolic risk factors after 6 months of observation: TC (by 44.01%, p<0.05), LDL (by 52.90%, p<0.05), IL-6 (by 27.52%, p<0.05), CRP (by 20.13%, p<0.05), TMA (by 14.66%, p<0.05), TMAO (by 33.91%, p<0.05), and significant increase in TMA/TMAO (by 23.45%, p<0.05), but the group with long-term postbiotics supplementation got better values.

Limitations of the study

The lack of prior research on the topic is the main study limitation.

Prospect of further research

The influence of investigated postbiotic combination (propionic acid and glycine) on patients' life quality and quantity of further cardiovascular events will be an interesting further studies topic.

Conflicts of interest is absent.

Acknowledgments

The study was done according to the department's scientific research work "Changes in protein. carbohydrate and lipid metabolism in patients with coronary heart disease and arterial hypertension with heart rhythm disorders. possibilities of drug correction" 2021–2023 (state registration number 0121U108875).

References

1. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42(5):373-498. DOI: 10.1093/eurheartj/ehaa612. Erratum in: Eur Heart J. 2021;42(5):507. DOI: 10.1093/eurheartj/ehaa798. Erratum in: Eur Heart J. 2021 Feb 1;42(5):546-7. DOI: 10.1093/eurheartj/ehaa945. Erratum in: Eur Heart J. 2021 Oct 21;42(40):4194. DOI: 10.1093/eurheartj/ehab648. PMID: 32860505.

2. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al.; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41(3):407-77. DOI: 10.1093/eurheartj/ehz425. Erratum in: Eur Heart J. 2020 Nov 21;41(44):4242. DOI: 10.1093/eurheartj/ehz825. PMID: 31504439.

3. Li JJ, Liu HH, Li S. Landscape of cardiometabolic risk factors in Chinese population: a narrative review. Cardiovasc Diabetol. 2022;21(1):113. DOI: 10.1186/s12933-022-01551-3. PMID: 35729555.

4. Rahman MM, Islam F, -Or-Rashid MH, Mamun AA, Rahaman MS, Islam MM, et al. The Gut Microbiota (Microbiome) in Cardiovascular Disease and Its Therapeutic Regulation. Front Cell Infect Microbiol. 2022;12:903570. DOI: 10.3389/fcimb.2022.903570. PMID: 35795187.

5. Gawałko M, Agbaedeng TA, Saljic A, Muller DN, Wilck N, Schnabel R, et al. Gut microbiota, dysbiosis and atrial fibrillation. Arrhythmogenic mechanisms and potential clinical implications. Cardiovasc Res. 2022;118(11):2415-27. DOI: 10.1093/cvr/cvab292. PMID: 34550344.

6. Canyelles M, Borras C, Rotllan N, Tondo M, Escola-Gil JC, Blanco-Vaca F. Gut Microbiota-Derived TMAO: A Causal Factor Promoting Atherosclerotic Cardiovascular Disease? Int J Mol Sci. 2023;24(3):1940. DOI: 10.3390/ijms24031940. PMID: 36768264.

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

7. Nataraj BH, Ali SA, Behare PV, Yadav H. Postbiotics-parabiotics: the new horizons in microbial biotherapy and functional foods. Microb Cell Fact. 2020;19(1):168. DOI: 10.1186/s12934-020-01426-w. PMID: 32819443.

8. Tain YL, Hou CY, Chang-Chien GP, Lin S, Tzeng HT, Lee WC, et al. Reprogramming Effects of Postbiotic Butyrate and Propionate on Maternal High-Fructose Diet-Induced Offspring Hypertension. Nutrients. 2023;15(7):1682. DOI: 10.3390/nu15071682. PMID: 37049522.

9. Vrzackova N, Ruml T, Zelenka J. Postbiotics, Metabolic Signaling, and Cancer. Molecules. 2021;26(6):1528. DOI: 10.3390/molecules26061528. PMID: 33799580.

10. Rom O, Liu Y, Liu Z, Zhao Y, Wu J, Ghrayeb A, et al. Glycine-based treatment ameliorates NAFLD by modulating fatty acid oxidation, glutathione synthesis, and the gut microbiome. Sci Transl Med. 2020;12(572):eaaz2841. DOI: 10.1126/scitranslmed.aaz2841. PMID: 33268508.

11. Yang S, Zhao J, Liu X, Wang J, Gu M, Cai C, et al. Metabolomics Profiling Predicts Ventricular Arrhythmia in Patients with an Implantable Cardioverter Defibrillator. J Cardiovasc Transl Res. 2024;17(1):91-101. DOI: 10.1007/s12265-023-10413-6. PMID: 37556036.

12. Faizi N. Alvi Y. Biostatistics Manual for Health Research. Netherlands: Elsevier; 2023. 275 p. DOI: 10.1016/C2022-0-00374-3.

13. Minich DM, Brown BI. A Review of Dietary (Phyto)Nutrients for Glutathione Support. Nutrients. 2019;11(9):2073. DOI: 10.3390/nu11092073. PMID: 31484368.

14. Janeiro MH, Ramirez MJ, Milagro FI, Martínez JA, Solas M. Implication of Trimethylamine N-Oxide (TMAO) in Disease: Potential Biomarker or New Therapeutic Target. Nutrients. 2018;10(10):1398. DOI: 10.3390/nu10101398. PMID: 30275434.

15. Wu JH, Batist G. Glutathione and glutathione analogues; therapeutic potentials. Biochim Biophys Acta. 2013;1830(5):3350-3. DOI: 10.1016/j.bbagen.2012.11.016. PMID: 23201199.

16. Huang P, Huang Y, Lv B, Zhang H, Liu J, Yang G, et al. Endogenous Taurine Downregulation Is Required for Renal Injury in Salt-Sensitive Hypertensive Rats via CBS/H2S Inhibition. Oxid Med Cell Longev. 2021;2021:5530907. DOI: 10.1155/2021/5530907. PMID: 34484563.

17. Lurz E, Horne RG, Maattanen P, Wu RY, Botts SR, Li B, et al. Vitamin B12 Deficiency Alters the Gut Microbiota in a Murine Model of Colitis. Front Nutr. 2020;7:83. DOI: 10.3389/fnut.2020.00083. PMID: 32582756.

18. Lyzohub VH, Kramarova VN, Melnychuk IO. Role of intestinal microbiota changes in cardiovascular diseases pathogenesis. Zaporozhye Medical Journal. 2019;(5):672-8. DOI: 10.14739/2310-1210.2019.5.179462.

19. Krueger ES, Beales JL, Russon KB, Elison WS, Davis JR, Hansen JM, et al. Gut Metabolite Trimethylamine N-Oxide Protects INS-1 β-Cell and Rat Islet Function under Diabetic Glucolipotoxic Conditions. Biomolecules. 2021;11(12):1892. DOI: 10.3390/biom11121892. PMID: 34944536.

20. Vacca A, Schiattarella GG. From Gut to Heart: Role of Indole-3-Propionic Acid in HFpEF. Circ Res. 2024;134(4):390-2. DOI: 10.1161/CIRCRESAHA.123.323947. PMID: 38359099.

Мельничук І.О., Крамарова В.Н.

ВПЛИВ ДОВГОТРИВАЛОГО ПРИЗНАЧЕННЯ ПОСТБІОТИКІВ НА КАРДІОМЕТАБОЛІЧНІ ФАКТОРИ РИЗИКУ У ПАЦІЄНТІВ З ІШЕМІЧНОЮ ХВОРОБОЮ СЕРЦЯ ТА МИГОТЛИВОЮ АРИТМІЄЮ

Метою дослідження була оцінка впливу тривалого призначення постбіотиків на КардіоМетаболічні Фактори Ризику (КМФР) у пацієнтів з Ішемічною Хворобою Серця (ІХС)

ISSN print 2414-4495, ISSN online 2710-1444, https://msz.knmu.edu.ua, msz.journal@knmu.edu.ua

та Фібриляцією Передсердь (ФП). 124 пацієнти з ІХС та пароксизмом ФП були розподілені стратифікованою рандомізацією 1:3 на дві групи: I (31 пацієнт) та II (93 пацієнти). Стратифікацію проводили за віком, статтю, індексом маси тіла та Загальним Холестерином (ЗХ) пацієнта. Усі пацієнти отримували стандартну терапію (СТ), згідно з останніми рекомендаціями Європейського товариства кардіологів. В I групі призначали СТ і постбіотики протягом 6 місяців: ребаміпід (2-(4-хлорбензоламино)-3-[2(1H))-хинолон-4] пропіонова кислота) (100 мг 3 рази на добу) та гліцин (100 мг 3 рази на день). Хворі II групи отримували лише СТ. Всі хворі були обстежені двічі: під час первинного обстеження та через 6 місяців лікування. Після лікування у I групі спостерігалося достовірне ($p<0,05$) зниження ЗХ (на 10,00 %), ЛіпоПротеїнів Низької Щільності (ЛПНЩ) (на 19,50 %), аполіпопротеїну В (на 12,92 %), ІнтерЛейкіну-6 (ІЛ-6) (на 12,40 %), С-Реактивного Білку (СРБ) (на 15,89 %), ТриМетилАміну (ТМА) (на 19,32 %), ТриМетилАмін-N-Оксиду (ТМАО) (на 27,24 %), порівняно з II групою. Після лікування у всіх пацієнтів виявили достовірне ($p<0,05$) зниження КМФР: ЗХ (на 44,01 %,), ЛПНЩ (на 52,90 %), ІЛ-6 (на 27,52 %), СРБ (на 20,13 %), ТМА (на 14,66 %), ТМАО (на 33,91 %), значне збільшення ТМА/ТМАО (на 23,45 %), хоча в I групі були досягнуті кращі значення. Отже, тривале (6 місяців) призначення постбіотиків (пропіонової кислоти та гліцину) має виражений позитивний вплив на КМФР у пацієнтів з ІХС та ФП.

Ключові слова: *гліцин, пропіонова кислота, аритмія, серцево-судинні розлади, дисліпідемія, запалення.*

Надійшла до редакції 08.02.2024

Information about the author

Melnychuk Iryna – MD, PhD, associate professor, Internal Medicine Department No.4, Bogomolets National Medical University, Kyiv, Ukraine.
Address: Ukraine, 01601, Kyiv, Tarasa Shevchenko Blvd, 13.
E-mail: ira.merkulova45@gmail.com
ORCID: 0000-0002-0659-1476.

Kramarova Viktoriia – MD, PhD, professor, Internal Medicine Department No.4, Bogomolets National Medical University, Kyiv, Ukraine
Address: Ukraine, 01601, Kyiv, Tarasa Shevchenko Blvd, 13.
E-mail: viktoriia.kramarova@gmail.com
ORCID: 0000-0003-2978-3320.