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The new possibilities of dietary correction of residual lipid metabolism disorders in patients with coronary artery disease and obesity

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Objective

To estimate the dynamics of lipid panel in patients with coronary artery disease (CAD), obesity and residual dyslipidemia, who receive optimal statin therapy and follow standard low-calorie diet with additional lipid-lowering product (LLP).

Materials and methods

This study included 40 patients with severe coronary atherosclerosis manifestations, who were selected for surgical revascularization of myocardium due to multiple vascular lesions and / or stenosis of proximal segments of

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the coronary arteries and with non-target atherogenic lipoproteins levels during optimal statin therapy. We also estimated additional effect of standard low-calorie diet (LCD) and LLP on the lipid panel.

Results

The results showed that 30-days follow-up of LCD could significantly decrease total cholesterol (TC) level by 15,7% (p=0,0003) and low-density lipoproteins (LDL) by 19,1% (p=0,0024), and the additional intake of LLP increased the efficiency of LCD and contributed to the achievement of reliable reduction of TC by 32.9% (p<0.0001), LDL by 38.1% (p<0.0001), very low density lipoproteins (VLDL) by 44, 5% (p= 0.013) and atherogenic coefficient of 35.2% (p= 0.003).

Conclusion

Based on the obtained results we can conclude that low-calorie diet for the correction of residual dyslipidemia during the standard statin therapy was superior to statin therapy potentiation and was associated with lower drug-loading.

Key words: *coronary artery disease, lipid metabolism, diet, obesity.*

Conflict of interests: None declared.

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Introduction

Coronary artery disease (CAD) is the major cause of death and disability in developed countries [1]. It should be emphasized that Russia is the leading country by the matter of CAD morbidity and mortality — the prevalence is 13,5% [2,3].

Modern approach to the pathogenesis of coronary artery disease is based on the idea of progressive occlusion of coronary arteries that develops over decades in response to the biological effects of various risk factors [4–6]. Hydroxymethylglutaryl-CoA reductase inhibitors (statins) are the basic modern treatment of atherosclerosis with powerful evidence base for their effectiveness for both primary and secondary prevention of the clinical manifestations of atherosclerosis [7,8]. At the same time, the indications fordrug treatmentare constantly expanding in evidence-based medicine, and decreasing fornon-drug approaches at the same time. However, there are still many issues on the treatment of CAD. Therefore, non-drug therapy is very promisingwhen used together with traditional statin therapy. The search for evidence of the efficacy of such approaches is extremely relevant nowadays.

The residual risk of cardiovascular complications in patients receiving optimal statin therapy is an issue of increasing concern. These patients cannot to achieve target values of atherogenic lipoproteins, including low density lipoproteins (LDL), despite receiving therapeutic doses of statins. Most often, high residual dyslipidemia occurs in patients with obesity, and, therefore, is associated not only with the presence of severe metabolic disorders, but also with factors limiting the use of high statins doses, such as non-alcoholic fatty liver disease and steatohepatitis [9].

These patients are in need for new approaches that potentiate the effect of basic lipid-lowering therapy. Such approaches include both pharmacological and non-pharmacological treatment strategies. Pharmacological strategies include, for example, ezetimibe, bile acid sequestrants and some other drugs. However, these approaches are associated with high drug loading and have very limited effectiveness. Many cardiologists see hopes in the new class of targeted drugs, such as evalocumab, that consists of monoclonal antibodies to PCSK9 that decreases the number of LDL receptors [10,11]. The major disadvantage is their high cost.

Dietotherapy (DT) is the most effective and leading non-pharmacological treatment method. At the same time DT cannot be considered as an alternative for statins therapy thath as proven its effectiveness in many studies. However, it has been proven that adequate DT can significantly decrease the level of atherogenic lipids, and in some cases even reduce the dosage of statins [12].

A modern approach to DT is the use of lipid-lowering products (LLP) with known chemical composition enriched with lipotropic components.

Based on the analysis of published data, it is interesting to confirm the effect of new LLP in clinical

practice as an independent nutritional factor for the correction of blood lipid profile disorders in patients with CAD receiving optimal statin therapy.

The objective of this study was to estimate the dynamics of lipid panel characteristics in patients with CAD, obesity and residual dyslipidemia, who receive optimal statin therapy and follow standard low-calorie diet with additional lipid-lowering product.

Materials and methods

An open prospective observational study was carried out on the basis of the Department of Cardiovascular Pathology of Federal State Scientific Institution "Federal Research Centre of Nutrition, Biotechnology and Food Safety" from October 15, 2016 to March 15, 2017.

Characteristics of patients. The study included patients with severe manifestations of coronary atherosclerosis, selected for surgical myocardial revascularization due to multiple vascular lesions and/or stenosis of proximal segments of the coronary arteries. Inclusion criteria were non-target LDL values (over 1.5 mmol / L) during optimal statin therapy (rosuvastatin over 20 mg / day, atorvastatin and simvastatin over 80 mg/day), body mass index (BMI)> 30 kg/m^2.

Given the non-interventional nature of this study, it was governed by the approval of the Ethics Committee of the Federal Research Centre of Nutrition, Biotechnology and Food Safety. All patients were informed of the purpose and nature of the observation and signed informed consent prior to the study. Patients were randomized into two groups by the method of nutritional treatment.

The study included 40 patients meeting the inclusion criteria. Age characteristics and clinical status of all participants are presented in Table 1. Most patients had severe cardiac status: 45–50 % of patients had class III angina, 85–90 % patients revealed arterial hypertension (AH), 35–50 % had clinical manifestations of chronic heart failure (CHF); 35–45 % of patients had non-alcoholic fatty liver disease (NAFLD).

The study follow-up was 30 days and included 3 observation points.

Point 1 (Day 1). On the day of admission, in accordance with the study protocol, patients underwent physical examination, anthropometric, body composition studies, a 6-minute walk test, a study of energy expenditure and fats oxidation rates, proteins and carbohydrates metabolism, and blood sampling.

Point 2 (Day 15). A blood sampling was performed to analyze the blood lipid profile.

Table 1. **Characteristic of studied groups**

Parameters	Studied groups (M±m)	
	Main group	Control group
Number of patients	20	20
Gender, anatomical and age characteristics		
Average age, years	63.08±4.69	61.1±9.9
Men	9	10
Women	11	10
BMI, kg/m^2	39.9±4.4	36.7±5.0
Class of angina		
I (% of patients)	3 (15 %)	2 (10 %)
II (% of patients)	7 (35 %)	9 (45 %)
III (% of patients)	10 (50 %)	9 (45 %)
IV (% of patients)	0	0
Comorbidities		
I–III grade arterial hypertension	18 (90 %)	17 (85 %)
Clinical manifestations of Chronic Heart Failure with over 2ndFunctional Class (% of patients)	10 (50 %)	7 (35 %)
Type 2 diabetes mellitus	13 (65 %)	15 (75 %)
NAFLD (% of patients)	7 (35 %)	9 (45 %)

Point 3 (Day 30) On the day of discharge. Patients underwent anthropometric studies, a study of body composition, basal metabolism, and blood sampling.

Patients from the main group (MG) (N=20) received a standard low-calorie diet (LCD) for 30 days with the additional LLP of 36 g / day (174.6 kcal/day).

Patients from the control group (CG) (N=20) — received LCD only for 30 days.

LCD is a diet with significant reduction of fats and easily digestible carbohydrates, normal protein and complex carbohydrates with increased amount of dietary fiber. Salt is usually limited (3–5 g/day). Dishes should be steamed, stewed, baked, mashed or not mashed. Food temperature — from 15 ° to 60–65 °C. Fluid consumption — 0.8–1.5 liters per day. Fractional nutrition — 4–6 times a day. Chemical composition: proteins — 70–80 g, including animal proteins — 40 g; general fats — 60–70 g, including vegetable — 25 g; total carbohydrates — 130–150 g, dietary fiber —30 g. Energy value: 1350–1550 kcal.

LLP "Dietary Oil" ("SOYUZ-M") is a fat product with the additional skimmed milk powder, with a mass fraction of fat of 53 %. The fatty acid (FA) composition of the LLP "Dietary oil" is presented in table 2.

Chemical composition of both group's diets are presented in table 3.

Biochemical studies were performed using «Konelab 30i» analyzer (ThermoClinicalLabsystems, Finland). Biochemical markers of lipid metabolism were total cholesterol (TC), (⩽ 5.0 mmol/L), triglycerides (TG), (⩽ 1.7 mmol/L), high density lipoprotein cholesterol (HDL) (⩽ 1.0 mmol/L). Very low-density

Table 2. **The fatty acid composition of the LLP "Dietary oil"**

FA name	FA index	FA composition, %
Caprylic	8:0	0.15
Capric	10:0	0.14
Lauric	12:0	2.29
Myristic	14:0	1.57
Palmitic	16:0	35.74
Hexadecenoic	16:1	0.04
Palmitoleic	16:1 7-cys	0.14
Margaric	17:0	0.10
Heptadecene	17:1	0.04
Stearic	18:0	4.44
Elaidic	18:1 9-trans	1.83
Oleic	18:1 9-cys	36.05
Vaccenic	18:1 11-trans	0.89
Iso-octadecanoic	18:2i	0.11
Linoleic	18:2	14.13
γ-linolenic	18:3 ω-6	0.09
α-linolenic	18:3 ω-3	0.90
Arachidonic	20:0	0.48
Gondoic	20:1	0.18
Eicosapentaenoic	20:5	0.23
Docosapentaenoic	22:5	0.07
Docosahexaenoic	22:6	0.35

Table3. **The comparison of the chemical composition of LCD and a modified diet with additional LLP**

Diet composition parameters	LCD	LCD+LLP
Energyvalue, kcal / day	1350–1550	1524,6–1724,6
Proteins, g/day	70–80	70,2–80,2
Fats, g/day	60–70	79–89
Carbohydrates, g/day	130–150	130,3–150,3

lipoprotein cholesterol (VLDL) was determined by dividing the number of TG by 2.2 (l⩽ 0.77 mmol / L); low density lipoprotein cholesterol (LDL) by subtracting the summary of HDL and VLDL from the amount of TC (⩽ 2.8 mmol/l). The atherogenic coefficient (AC) was calculated by the formula of A.N. Klimova (⩽ 3.5 mmol/l).

Statistical analysis was performed using the STATISTICA 10.0 software. When analyzing the main characteristics of patients, parametric criteria were used, and the data are presented as mean± standard deviation or % of the total number of patients. The significance level was set as p<0.05.

Results and discussion

The results of the analysis of blood lipid spectrum dynamics are presented in table 4. Initially, both groups had average lipid profile parameters levels within the reference (but not target) values. Atherogenic lipid fractions were comparable between groups: the level of TC in patients from the MG was 5.47± 0.85 mmol / l, from the CG — 5.71± 1.13 mmol/l (p= 0.463); the level of LDL in MG was 3.62± 0.69 mmol/l, in CG — 3.56± 1.03 mmol / l (p= 0.823), the level of VLDL in the MG was 0.83± 0.57 mmol/l, in CG — 0.81± 0.35 mmol / l (p= 0.89), that allowed to analyze its dynamics. At the same time, the HDL and TG levels between groups were not comparable (HDL: in the MG — 1.05± 0.28 mmol / l, in the CG — 1.49± 0.33 mmol / l, p= 0077) (TG: in the MG= 3.03± 0.80 mmol/l., in the CG= 1.42± 0.49 mmol/l, p<0.01), and, therefore, these indicators were not included in the subsequent analysis.

The analysis of TC level revealed its significant decrease in patients with low-calorie diet (Fig. 1, 2). At the same time, additional inclusion of LLP into the diet allowed to obtain an additional reduction of TC: in patients from the MG the level of TC decreased by 1.13± 0.56 mmol / L (–20.3%, p<0.0001) in 2 weeks, and by 1.80± 1.09 (–32.9%, p<0.0001) in 4 weeks, while in patients from the CG its level only had insignificant tendency to decrease by 0.15± 0.46 mmol/l (p= 0.16) in 2 weeks of treatment and significantly decreased by 0.90± 0.93 mmol/L (–15.7%, p= 0.0003) in 4 weeks.

The intergroup statistical analysis found that the differences were highly significant at the second and third observation points: after 2 weeks the level of total cholesterol in the MG was 4.34± 0.58 mmol/l, in CG — 5.56± 0.79 mmol / l (p<0.0001), after 4 weeks: in

Table 4. **The comparison of blood lipid spectrum parameters during treatment**

Blood lipid spectrum parameters	Initially			After 2 weeks			After 4 weeks		
	MG	CG	p	MG	CG	p	MG	CG	p
TC, mmol/l	5.47±0.85	5.71±1.13	0.463	4.34±0.58	5.56±0.79	<0.0001	3.67±0.73	4.80±0.64	<0.0001
LDL, mmol/l	3.62±0.69	3.56±1.03	0.823	2.68±0.51	3.25±0.71	0.006	2.24±0.72	2.88±0.59	0.003
HDL, mmol/l	1.05±0.28	1.49±0.33	0.007	0.98±,25	1.37±0.31	0.0008	0.99±0.18	1.20±0.31	0.015
VLDL, mmol/l	0.83±0.57	0.81±0.35	0.88	0.59±0.21	0.79±0.34	0.029	0.45±0.22	0.71±0.35	0.009
TG, mmol/l	3.03±0.80	1.42±0.49	<0.01	2.22±0.37	1.49±0.50	<0.0001	1.86±0.60	1.51±0.80	0.124
AC, kg/m^2	2.21±0.81	2.04±0.85	0.52	1.77±0.57	1.95±0.74	0.4	1.42±0.72	1.94±0.90	0.05

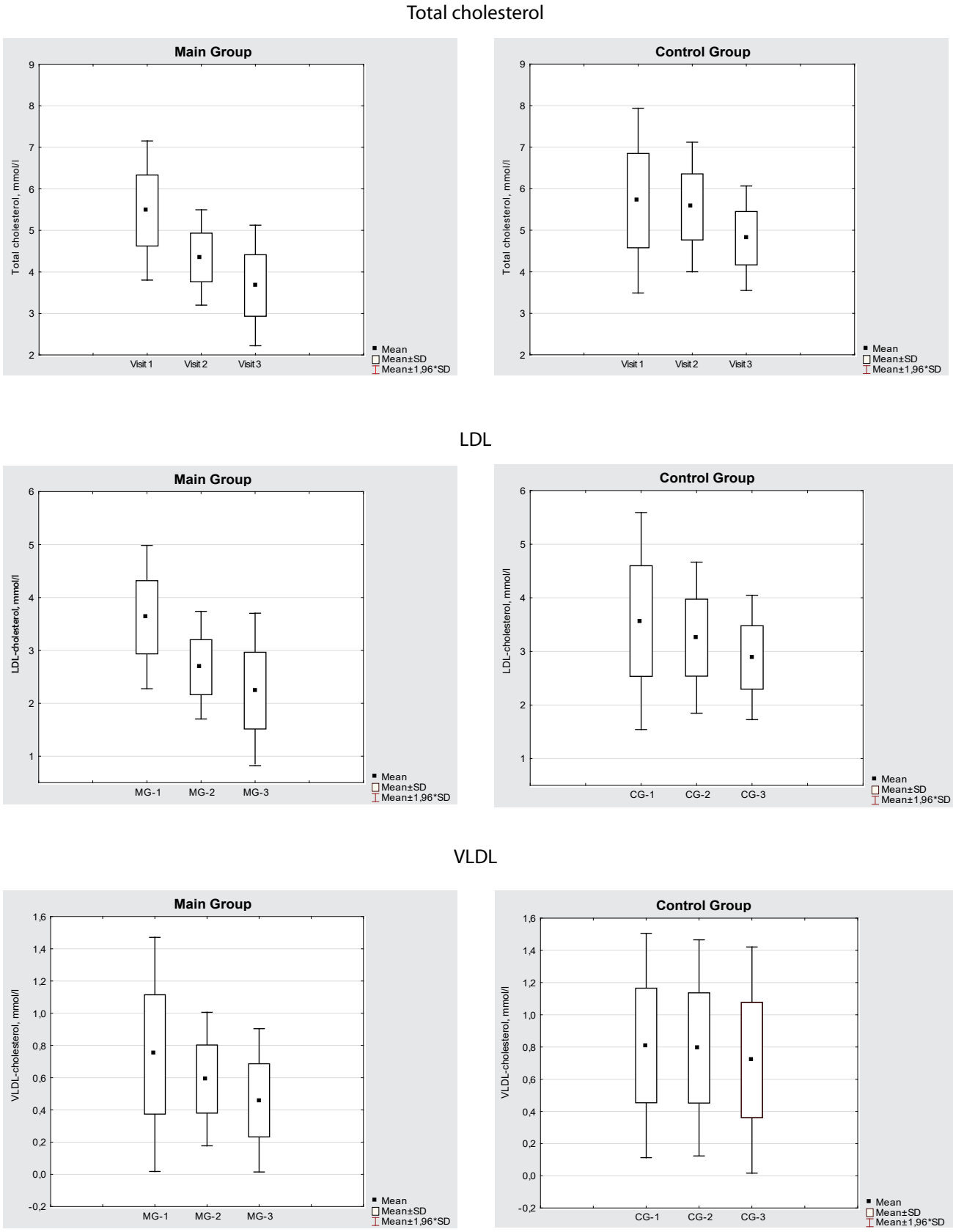
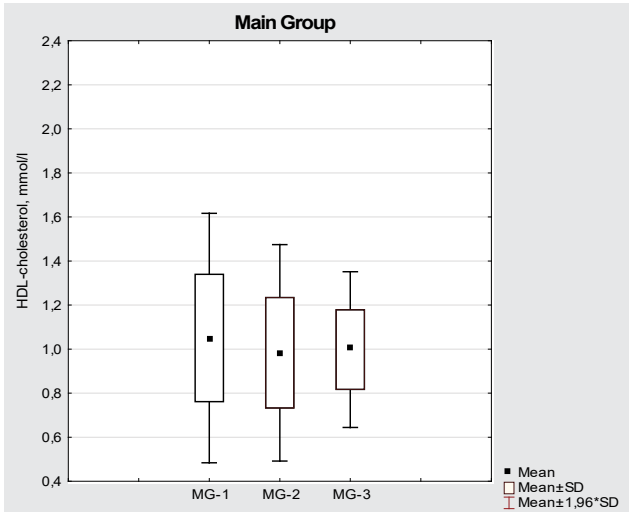
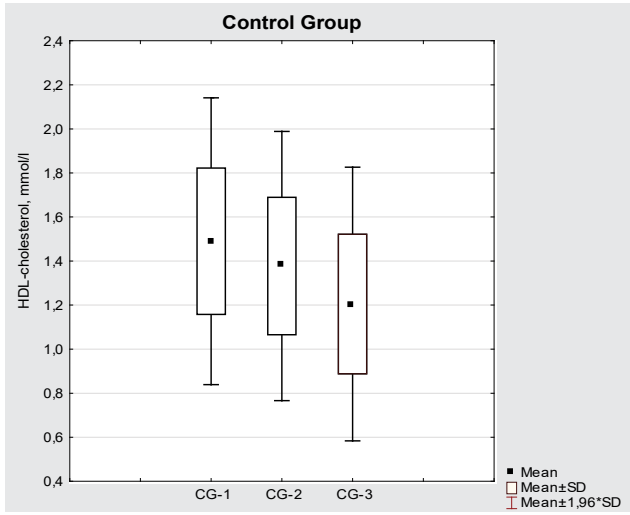


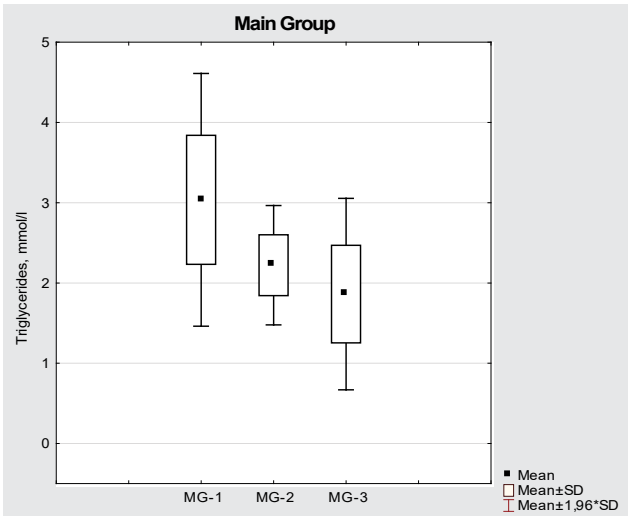
Figure 1. Diagrams of lipid spectrum parameters in patients during treatment

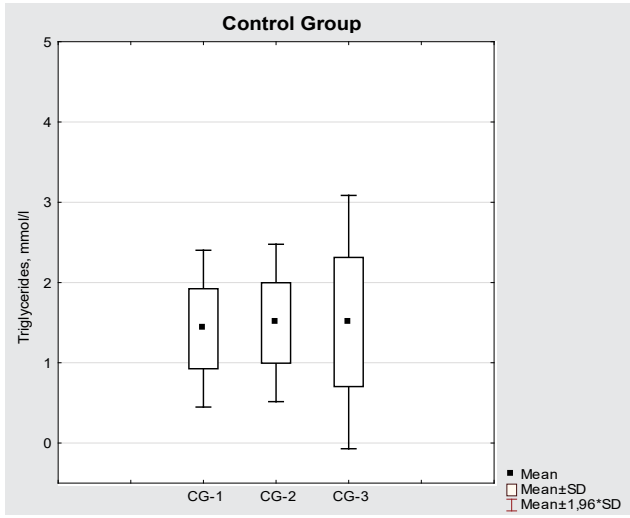
HDL



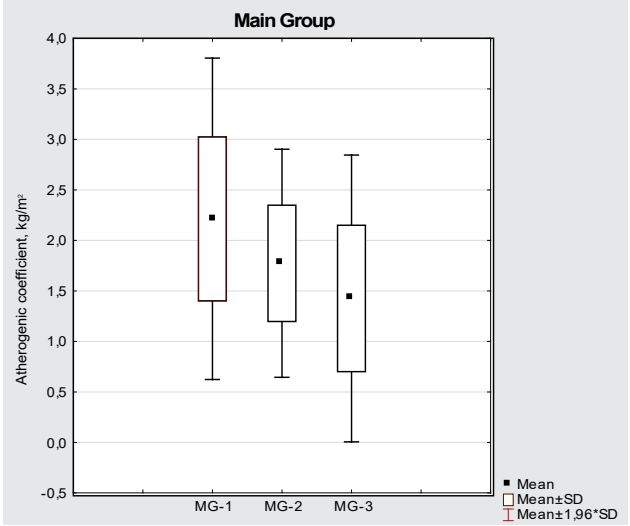


TG





AC



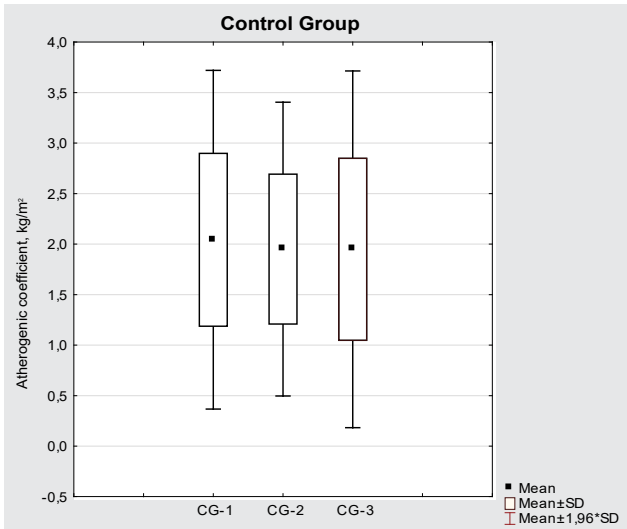


Figure 2. (continuation) Diagrams of lipid spectrum parameters in patients during treatment

MG — 3.67± 0.73 mmol / l, in CG — 4.80± 0.64 mmol/l (p<0.0001).

Average LDL values, despite the ongoing DT, were higher than the target values during the entire observation period, thus, it was not possible to achieve the main goal of diet therapy during this study. At the same time, different nutritional approaches have shown different levels of efficacy. Standard LKD revealed the decrease of LDL by 0.31± 0.43 mmol/L (8.7 %, p= 0.0046) in 2 weeks andin 4 weeks — by 0.68± 0.87 mmol / L (19.1 %, p= 0.0024). The additional LLP intake showed even more pronounced reduction of LDL level — by 0.94± 0.48 mmol / L (–25.9 %, p<0.0001) in 2 weeks and by 1, 38±0.96 (–38.1 %, p<0.0001) in 4 weeks.

Intergroup statistical analysis revealed significant differences during the dynamic observation: at the second observation point the values were 2.68± 0.51 and 3.25± 0.71 mmol / L in the MG and CG, respectively (p= 0.006), at the third point — 2, 24±0.72 and 2.88± 0.59 mmol / L, with p= 0.003.

The dynamics of VLDL level were similar to LDL. VLDL level decreased in both groups during treatment: in the MG it decreased in 2 weeks by 0.24± 0.40 (–28.9 %, p= 0.015) mmol / L and amounted to 0.59± 0. 21 mmol / L, and in 4 weeks — by 0.37± 0.61 mmol/L (–44.5 %, p=0.013) and amounted to 0.45± 0.22 mmol / L. In the CG, the level of VLDL did not change significantly during the entire observation period — there was only tendency to decrease in 2 weeks by 0.015± 0.1 mmol / L (p= 0.5), and in 4 weeks — by 0.09± 0.2 mmol / l (p= 0.058).

Intergroup statistical analysis revealed significant differences in VLDL level, after 2 (at p= 0.029), and 4 (p= 0.009) weeks of treatment.

The analysis of the AC dynamics showed its significant decrease in the MG, as well as the presence of a strong tendency (but unreliable) to decrease in the CG. In the MG, it decreased after 2 weeks from 2.21± 0.81 kg / m^2 to 1.77± 0.57 kg / m^2 — by 0.44± 0.58 kg / m^2 (–19.9 %, p= 0.003), and after 4 weeks — up to 1.42± 0.72 kg / m^2 (–35.2 %, p= 0.003). In the CG, the AC value decreased insignificantly by 0.09± 1.1 kg / m^2 (p= 0.3) and did not change by the end of the observation.

Conclusion

The results obtained in this study allow us to conclude that it should be recommended to use the possibilities of both low-calorie diet and LLP with anti-atherogenic effect in patients with coronary artery disease, obesity, and non-target atherogenic lipoproteins level during standard statin therapy. This approach allows achieving an additional decrease in LDL by more than 44 % without increasing the drug load that is potentially more effective than using other lipid-lowering medications — cholesterol absorption inhibitors or sources of highly purified polyunsaturated fatty acids of the omega-3 family.

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