Atherosclerosis and Dyslipidaemias
An official Journal of the Russian National Atherosclerosis Society (RNAS)
2018 №1
ABSTRACTS

Statins in routine clinical care in elderly with hyperlipidemia and coronary heart disease. Russian program EFFORT

M. G. Bubnova, D. M. Aronov, A. D. Deev*

National medical research Center for Preventive Medicine, Ministry of Health of the Russian Federation, Moscow, Russia

* List of participants:
Yekaterinburg (I. S. Baratz, I. A. Batanova, Yu. O. Verkhovtseva, A. P. Getmanov, N. C. Dymbrylova, L. G. Zhelomskaya, I. A. Eremenko, N. V. Izmozherova, I. V. Petrova, E. R. Prokopyeva, S. Yu. Pulatova, N. N. Silkina, A. Yu. Stepanova, E. M. Hurs, S. N. Shilonosov); Kazan (I. N. Arsentieva, R. V. Akhmetzyanov, G. Kh. Kalimullina, T. A. Nabiullina, G. Kh. Sadreev, N. M. Shakirov, Yu. P. Shamitov, I. G. Yakovleva) ; Moscow and Moscow Region (Yu. V. Artamonova, Sh. V. Akhadov, E. A. Ashurkova, A. A. Bazarnova, E. A. Bezlyudova, M. R. Buziashvili, O. V. Glushenkova, E. V. Gorbacheva, O. I. Didenko, T. I. Zakharova, D. S. Islamova, M. S. Jormark, L.Yu. Kulagina, I. V. Molchanova, I. A. Novichikhina, F. N. Paleev, S. A. Rokina, O. V. Sabitova, A. N. Sadchikova, T. Yu. Titova, O. A. Furman, E. A. Tselikh, I. V. Chugunova, T. V. Shashkova, E. I. Yakovenko); Krasnodar (Yu. V. Arkhipova, O. A. Alukhyanyan, G. S. Arustamyan, M. I. Ivochkina, N. V. Klimenko, L. N. Klykova, M. V. Kolodina, E. D. Kosmacheva, O. A. Lebed, L. L. Machkalyan, L. N. Sirotenko, T. V. Tarasova, S. N. Tyshkevich, I. Yu. Khut, N. V. Yurina); Novosibirsk (E. V. Antonova, E. N. Bagdulina, N. V. Korotina, A. A. Manuilova, S. V. Palapa, E. A. Pechenkina, I. V. Poshinova); Rostov-on-Don (N. B. Afanasyeva, S. V. Grebenyuk, V. S. Grishina, A. V. Kolosova, S. A. Lyashenko, I. I. Prostov, S. V. Sobin, G. O. Treneva, V. A. Yudin); St. Petersburg (N. I. Abaradzhi, L. M. Aleynikova, E. V. Bugaeva, L.Yu. Bushkova, N. M. Vasilyeva, L. B. Vasilieva, L. N. Varnakova, V. I. Gordina, A. K. Efimova, E. V. Kobelev, V. A. Kuzmina, E. A. Meldova, N. N. Omelchuk, I. V. Pekina, N. A. Petrochenko, I. G. Rishko, O. V. Samarina, I. Yu. Serdyuk, T. N. Sinotova, B. P. Stepanov, L. D. Strezhakova, M. A. Cylina, Yu. A. Shatova, V. V. Shchunik, A. G. Yamilova); Samara (V. Yu. Kapelovich); Stavropol (E. I. Lobzhanidze, O. Ponomareva); Tyumen (S. G. Berdinskikh, I. A. Velizhanina, A. M. Vershinina, M. A. Gibelgaus, I. I. Grigorenko, T. V. Dubova, I. A. Zhevagina, S. V. Zubayilova, O. V. Yevdakimova, N. Yu. Savelyeva, E. N. Semukhina, N. K. Shatyrko, N. P. Shurkevich, O. V. Yurerova).

Abstract
Aim. To investigate the use of statins and patients' adherence to statin therapy in elderly patients (pts) with hyperlipidemia (HL) and coronary heart disease (CHD) in real clinical practice.
Methods. The program was conducted in health care facilities from 2010 to 2011. 959 pts aged ± 65 yrs (mean age 68.9 ± 0.2 yrs) with HL and CHD were enrolled into the program. There were 47.5% women participating in the program.
Results. The high prevalence of coronary risk factors was revealed in cohort of elderly pts with HL and CHD: arterial hypertension (93%), left ventricular hypertrophy (82%), abdominal obesity (59%), type 2 diabetes mellitus (25%). 20.4% of pts were smokers and 97.7% were physical inactive. Myocardial infarction and stroke have experienced 31.6% and 9.1% of the pts, respectively. Statins were recommended for 77% of the elderly pts; 18.7% of them refused to take statins and 41.5% took them as courses. The main reasons for low adherence to statin therapy in elderly included fear of adverse reactions (46%); a lack of motivation to be treated (29.4%); polypragmasia (27.6%),

memory problems (26.5%), low-efficiency treatment (18.8%).Actually only 11.7% of the elderly pts, who had taken the statins refused to use it because of adverse events (AEs) being developed. There were mild and moderate muscular/tensions AEs in 9.2% of all pts and an asymptomatic creatine phosphokinase increase in 0.83%. The cost of the drug restricted it's use to only 13.5% of the elderly pts.

Conclusions. The Russian program EFFORT included a cohort of elderly pts has revealed the high prevalence of risk-factors among them and poor control, determined by low pts adherence to the statin therapy.

Keywords: statin, adherence, elderly.

The choice of species and lines of animals for evaluation of lipid-lowering medicines

M. N. Makarova, V. G. Makarov, S. V. Khodko

Research-and-manufacturing company "Home of pharmacy" Closed Joint-Stock Company, Saint Petersburg, Russia

Abstract

To date there are no effective means to stop the development of atherosclerosis, the major cause of ischemic cardiovascular diseases, a leading cause of death for people. The creation of anti-atherogenic and lipid-lowering drugs is possible only in the process of in-depth preclinical studies on experimental animals. Models of atherosclerosis should be similar in pathogenesis to atherosclerosis person and meet the following criteria: the similarity of the experimental nature of the violations with those; the similarity of the lipid profile of blood plasma and metabolism with the metabolism in the human body; rate of breeding animals and the development of atherosclerotic disorders; the cost of purchasing and maintaining animals; the ability to perform manipulation and visualization of disturbances in vivo and a number of others.

The review considers current approaches to the modeling of atherosclerosis in various species and lines of animals. Analysis of the literature suggests the possibility of using models of atherosclerosis such rarely used for these purposes, the types of animals like Guinea pigs, degus and hamsters that meet many of these criteria. It is also shown that for studying the mechanisms of atherosclerosis, including at the molecular level, optimally match the different lines of genetically changed rodents, in particular mice. However, for the study of new drugs anti-atherogenic and lipid-lowering drugs requires larger animals (Guinea pigs, degus and hamsters), suitable for long-term dynamic observation, which requires regular blood sampling. Due to the fact that so far there is no single model of atherosclerosis in animals, which would satisfy all the required criteria, should, apparently, in preclinical studies to use as small animals (guinea pigs, hamsters, degus) for preliminary rapid tests, and large (rabbits, dwarf pigs) to confirm the effectiveness of pharmacological drugs.

Keywords: atherosclerosis, experimental model, animal species.

The correlation between intima-media complex, ankle brachial indexes and dyslipidemia with coronary heart disease among urbanized and non-urbanized population of Gornaya Shoria

E. V. Mihalina[1], T. A. Mulerova[1, 2], A. A. Kuzmina[1], M. Yu. Ogarkov[1, 2]

1 Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russia
2 Novokuznetsk State Institute of Advanced Medical Training, Ministry of Health of the Russian Federation, Novokuznetsk, Russia

Abstract

Objective: to assess the relationship of the value of the intima-media complex (IMC), ankle brachial indexes (ABI) and dyslipidemia with coronary heart disease (CHD) among residents of Gornaya Shoria depending on the level of urbanization.
Material and methods. Clinical and epidemiological study of indigenous Gornaya Shoria (sample of 513 people, including 265 residents of Sheregesh (urban-type settlement) and 248 residents of Orton and Ust- Kabyrzy (hard to reach remote villages of Gornaya Shoria)).
We studied the lipid spectrum of the blood. We measured blood pressure (BP), calculation of IMC on the carotid arteries, ABI was calculated. CHD was exhibited on the basis of the criteria of the Minnesota code, profiles Rose and anamnesis.
Results: the prevalence of CHD among the urban and rural population of Gornaya Shoria was 14.11% and 11.75% respectively, which is comparable with the average. Indigenous people living in rural areas had higher levels of triglycerides (TG), and Shorians, living in the city a higher level of low-density lipoprotein cholesterol (LDL-C). Among the urban population were more common individuals with elevated levels of IMC compared with the rural population. Shorians, living in rural areas had lower levels of ABI than urban residents. Among the urban population with coronary artery disease had greater number of people with elevated levels of LDL-C. Regardless of the level of urbanization higher IMC observed in patients with coronary artery disease.
Keywords: intima-media, ankle-brachial index, shorians, coronary heart disease.

Spectrum of fatty acids, lipids and markers of inflammation in patients with coronary atherosclerosis

Ya. V. Polonskaya[1], V. S. Shramko[1], S. V. Morozov[2], E. I. Chernyak[2], A. M. Chernyavskiy[3], Yu. I. Ragino[1]

1 Scientific Institution of Internal and Preventive Medicine, Novosibirsk, Russia
2 N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry Of Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russia
3 Federal State Budgetary Institution "National Medical Research Center named acad. E. N. Meshalkin" of the Ministry of Health of the Russian Federation, Center for surgery of aorta, coronary and peripheral arteries, Novosibirsk, Russia

Abstract
Research purpose. Study of the balance of unsaturated fatty acids and their associations with indicators of lipid metabolism and markers of inflammation in men with coronary atherosclerosis.
Material and Methods. The study included 40 men aged 38–66 years. The basic group – 30 patients with verified coronary angiographic coronary atherosclerosis. The control group included 10 healthy men. In the serum was studied palmitoleic (16:1), oleic (18:1), linoleic (18:2 (ω-6)), α-linolenic (18:3 (ω-3)), γ-linolenic (18:3 (ω-6)), arachidonic (20:4 (ω-6)), eicosapentaenoic (20:5 (ω-3)) and docosahexaenoic (22:6 (ω-3)) acids. We calculated the coefficient ω-6/ω-3 polyunsaturated fatty acids. Determined the concentrations of tumor necrosis factor – α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), C-reactive protein (CRP), cholesterol, triglycerides, high density lipoproteins (HDL), peroxide oxidation of lipid.
Results. In patients with coronary atherosclerosis found a significant increase in the content of monounsaturated fatty acids – 18.2% ($p< 0.01$), triglyceride, peroxidation products, IL-6, IL-8 and CRP; and decrease in polyunsaturated fatty acids and HDL. In men with coronary atherosclerosis, the ratio of ω-6/ω-3 polyunsaturated fatty acids was 1.6 times higher (10.9/1 (84.23/7.74); $p< 0.05$) than in the control group. Correlation analysis revealed multiple relationships between the studied acids; with markers of inflammation –16:1, 18:1 and 18:3 (ω-6); triglycerides level – 16:1, 18:1, 18:2, 18:3 (ω-6) , 20:5 and 22:6; with cholesterol –16:1, 18:1, 18:2 and 18:3 (ω-3). Found a link palmitoleic (16:1) and oleic (18:1) with the presence of coronary atherosclerosis.

Conclusion. In coronary atherosclerosis observed pronounced changes in fatty acid composition and is accompanied by changes in lipid profile and markers of inflammation.
Keywords: coronary atherosclerosis, fatty acids, markers of inflammation, lipid metabolism.

The presence of small dense low-density lipoprotein subfractions in human serum induce the accumulation of cholesterol by monocyte-like THP-1 cells

O. I. Afanasieva[1], E. A. Utkina[1], E. B. Vikhrova[2], E. A. Klesareva[1], O. A. Razova[1], T. I. Arefieva[1], I. Ju. Adamova[1], S. N. Pokrovsky[1]

1 Laboratory of problems of atherosclerosis, Institute of Experimental Cardiology of "National Medical Research Center of Cardiology" Ministry of Health of the Russian Federation, Moscow, Russia
2 Pocard LTD, Moscow, Russia

Abstract
The aim of the study was to investigate the accumulation of total cholesterol (TC) in human macrophages depending on the subfractions' profile of apoB100-containing lipoproteins.
Materials and methods. THP-1 cells were incubated for 24 hours with human serum samples with TC level 240 mg/dl after macrophage differentiation. The supernatant was removed, the cells washed and lysed. The concentration of TC and total protein were measured by the colorimetric method in cell lysates.
The following data were determined in the sera: the concentration of lipoprotein fractions and subfractions by method of native polyacrylamide gel electrophoresis, B-100 apoprotein, circulating immune complexes (CIC), the content of oxidized low density lipoproteins (oxLDL) and titer of autoantibodies (autoAb) to oxLDL.
Results. Sera samples were divided into three groups depending on the concentration of subfractions of small dense low-density lipoproteins (sdLDL): group 1 – without sdLDL (n = 11); group 2 – with the concentration of sdLDL from 1 to 4.9 mg/dl (n = 13); group 3 – with the concentration of sdLDL ≥ 5 mg/dl (n = 11) – atherogenic profile B.
In the sera of group 3 relative to group 1, higher levels of apoB-100 (median, [25%, 75%] – 68.1 mg/dl [63.8, 84.1] and 58.6 mg/dl [43.9, 62.4], $p < 0.01$) and giant CICs (26.2 lab units [14.3, 31.8] and 11.3 lab units [9.7, 12.8], $p = 0.03$), were found respectively.
When cells were incubated in the presence of sera with an atherogenic profile B, the level of TC in the lysate normalized to the protein, was significantly higher than in the group without sdLDL (6.5 rel. units [3.9, 9.1] and 2.7 rel. units [2,1, 3.9], p= 0,03). The data of multivariate analysis with including into the model the values of TC, high-density lipoprotein cholesterol, apoB-100, oxLDL and medium size LDL particles (LDL-2) showed that only the concentration of sdLDL ($r = 0.709$, $p < 0.001$) worked as the independent predictor of accumulation of TC. When incubating the cells with the sera from patients with sdLDL concentration more than 1 mg/dl, the increased amount of TC in lysates was found even in the presence of the so-called non-atherogenic profile A.
Conclusion. The presence of sdLDL even in small (less than 5 mg/dl) concentrations and independently of other components of the blood serum causes the accumulation of cholesterol **by THP-1 cells.**
Keywords: small dense LDL, THP-1 cells, atherosclerosis, accumulation of cholesterol.

Prevalence of Dyslipidemia and Statins Use In Russian Acute Coronary Syndrome Registry

M. V. Ezhov[1], N. V. Lazareva[1], O. V. Sagaydak[1], V. A. Vygodin[2], U. V. Chubykina[1], S. A. Bliznyuk[1], I. A. Alekseeva[1], E. V. Oshchepkova[1]

1 “National Medical Research Center of Cardiology” Ministry of Health of the Russian Federation, Moscow, Russia
2 “National Medical Research Center for Preventive Medicine” Ministry of Health of the Russian Federation, Moscow, Russia

Abstract
Aim. The aim of this study was to describe lipid metabolism parameters and prevalence of severe hypercholesterolemia (LDL cholesterol≥5 mmol/l), as well as statin treatment in patients with acute coronary syndrome (ACS) included into Russian ACS registry.
Material and methods. This is a retrospective study based on data from Russian Registry of patients with ACS. Medical records and results of laboratory tests of lipid parameters from 924 patients hospitalized for ACS in 2015 were included in the analysis.
Results. The registry 2015 population comprised of 60% men, mean age was 65 ± 12 years, 27% people were younger than 60 years old. The prevalence of major cardio-vascular risk factors were as follows: arterial hypertension - 85%, hypercholesterolemia - 48%, type 2 diabetes - 17%. The mean levels of key lipid parameters at admission were: total cholesterol - 5.2 ± 1.4 mmol/L, triglycerides - 1.7 ± 1.0 mmol/L, high density lipoprotein cholesterol - 1.0 ± 0.2 mmol/L, low density lipoprotein (LDL) cholesterol 3.4 ± 1.2 mmol/L. The proportion of patients with severe hypercholesterolemia (potentially familial hypercholesterolemia) was 10%. Seventy percent of the 924 subjects included in the analysis had the medical history of cardiovascular disease (CVD), including 29% with documented myocardial infarction. Twenty percent of the total number of participants were on statin treatment at the time of admission. This proportion for patients with established CVD reached 30%. Only 9% of patients treated with statins had target level of LDL cholesterol at admission (<1.8 mmol/L).
Conclusion. Nearly half of Russian patients hospitalized for ACS has hypercholesterolemia at admission. Severe hypercholesterolemia was found in 10% of patients. Only 1/3 patients with established CVD and thus having class (I) recommendations for statins had the history of statins treatment before admission, and only 9% of them achieved the target level of LDL cholesterol. Urgent actions are needed for improvement of lipid lowering treatment in patients with ACS in Russia.
Keywords: registry, acute coronary syndrome, hypercholesterolemia, cardiovascular risk, statins, target level, low-density lipoprotein cholesterol.

Subcutaneous and visceral obesity in obese and underweight patients with cardiological profile

I.V. Logacheva[1], T. A. Ryazanova[1,2], V. R. Makarova[1,2], O. V. Surnina[2]

1 Izhevsk State Medical Academy, Izhevsk, Russia
2 Republician Clinical Diagnostic Centre, Izhevsk, Russia

Abstract
Goal. To study the features of subcutaneous and visceral obesity (VO) in relation to the body mass index (BMI) and to determine associative relationships between cardiometabolic risk factors (CFR) in men suffering from coronary artery disease (CAD) in combination with arterial hypertension (HA).
Materials and methods. We examined 90 male patients of metabolic unhealthy phenotype (MUP) diagnosed with cardiac ischemia and HA of 1–3 degrees, of median age 61.2 ± 1.7 years. Group I included 29 patients with IMB up to 25 kg/m2, group II – 31 overweight patients with BMI > 25 kg/m2, and in group III we had 30 obese patients with a BMI > 30 kg/m2, while the control group consisted of 30 patients with healthy metabolic phenotype (MHP). Anthropometric and ultrasound

indices of subcutaneous and visceral fat were studied, the thickness of intra-abdominal and epicardial fat (TIA/TEF) were assessed, indices of abdominal wall fat (AWF) and visceral obesity (VAI) were calculated and metabolic parameters (lipid profile and insulin resistance (HOMA-IR)) were determined. The magnitude of the intima – media complex (CIM) and endothelium dependent vasodilation (EDV) were assessed via the ultrasound.
Results. In all groups of patients with MUP, the thickness of subcutaneous fat did not differ significantly. Dyslipidemia, remodeling of the vascular wall, constriction of the brachial artery was observed in patients with a BMI <25 kg/m2, regardless of the thickness of subcutaneous fat.
All indicators reflecting the metabolic «unhealth» increased with increasing weight. In obese patients, higher figures of TIA/TEF and AWF (higher in group III, respectively, were 103.1 ± 5.2 / 10.4 ± 0.5 mm and 1.17 ± 0.1). BMI was associated with TIA and AWF only in obese patients ($p < 0.01$). With increasing weight, the parameters of vascular remodeling changed: the magnitude of CIM in groups II and III was 1.12 ± 0.08 and 1.17 ± 0.04 mm, vasoconstriction was recorded in 78.7% of obese patients. In obese patients, associative relationship between BMI and the magnitude of CIM, the indicators of EDV was revealed.
Conclusion. Visceral fat deposition in patients with cardiac pathology contributes to a significant increase of CRF, associated with each other and aggravating vascular remodeling. Diagnosis of VO using ultrasound, an alternative anthropometric technique, allows us to talk about TIA as one of the leading factors of metabolic risk. The BMI continues to serve as one of the criteria for a high CRF in the MUP.
Keywords: cardiac pathology, obesity, vascular remodeling.

Evolocumab had no effect in young women with familial hypercholesterolemia

K. S. Benimetskaya[1,2], K. V. Makarenkova[1], L. D. Latyntseva[1], O. V. Cigankova[1,3], S. V. Astrakov[2], E. V. Shakhtshneider[1], Yu. I. Ragino[1], M. I. Voevoda[1]

1 Research Institute of Internal and Preventive Medicine – Branch of Federal State Budget Scientific Institution The Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Science, Novosibirsk, Russia
2 Institute of Medicine and Psychology, Novosibirsk National Research State University (NSU), Novosibirsk, Russia
3 Department of emergency therapy with endocrinology and occupational pathology, Novosibirsk State Medical University, Novosibirsk, Russia

Abstract
Familial hypercholesterolemia is an autosomal dominant genetic disorder characterized by a significant increase of blood cholesterol level, premature development and progression of atherosclerosis. In case of homozygous form total cholesterol level exceeds 14 mmol/l. The article presents the case of absence of PCSK9 inhibitor effect in a young woman with familial hypercholesterolemia, compound heterozygous for the low density lipoprotein receptor gene, who needs therapy with PCSK9 inhibitors, according to the Russian guidelines on the diagnosis and treatment of familial hypercholesterolemia.
Keywords: familial hypercholesterolemia, compound heterozygous, low density lipoprotein cholesterol, atherosclerosis, xanthomatosis, PCSK9 inhibitors, evolocumab.

Report on the REAL-CAD study