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ABSTRACTS

Consensus Statement of the Russian National Atherosclerosis Society (RNAS) Familial hypercholesterolemia in Russia: outstanding issues in diagnosis and management

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Abstract

Lipid metabolism disorders play a pivotal role in increased mortality and morbidity from atherosclerotic cardiovascular disease throughout the world with familial hypercholesterolemia (FH) being the most common cause of premature death from coronary heart disease. In the Russian Federation, the estimated number of patients with heterozygous FH (heFH) is ~ 287 000, whereas it is assumed that there are about 150–300 patients with homozygous form (hoFH). However, the true prevalence of this disease is unknown in most countries, thus these patients with genetically elevated levels of low-density lipoprotein cholesterol are left without proper and timely management. While hoFH fully meets the criteria for a rare disease, in contrast heFH occurs 2 times more often than other hereditary diseases. Data analysis from British registry has shown that FH patients aged 20–39 have a 100-fold increase in risk of death from coronary events and a 10-fold increase in total mortality compared with the general population. HoFH patients without treatment die before the age of 20 years from complications of atherosclerosis. This document summarizes the opinion of experts on the matter of optimizing the detection and treatment algorithms of FH patients. The interim analysis of the Russian FH Register is presented. The consensus provides a rationale for the creation of the network of lipid centers in Russia and some other steps that need to be done for the improvement of the diagnosis and the treatment of FH.
Keywords: familial hypercholesterolemia, atherosclerosis, screening, diagnosis, treatment, apheresis, registry.

The role of oxidized low-density lipoproteins and antibodies against oxidized low-density lipoproteins in the immune and inflammatory process in atherosclerosis

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Abstract

Oxidized low-density lipoproteins (OxLDL) and antibodies against oxidized LDL (Anti-OxLDL) play a leading role in atherogenesis. OxLDL are one of the most studied autoantigens that induce a local immune response in the arterial wall. According to modern concepts, oxidative modification of low-density lipoproteins (LDL) converts them into a form gripped by macrophages more faster than native LDL, that contributes to the progression of the atherosclerotic process. Levels of OxLDL may have prognostic value in relation to the cardiovascular risk. AntiOxLDL can be considered markers of LDL oxidation and independent predictor of atherosclerotic progression. The level of Anti-OxLDL could be linked with the rate of atherosclerotic lesions in the coronary, carotid and peripheral arteries. This review summarizes current data on oxidative modification of LDL and the role of OxLDL and Anti-OxLDL in the immuno-inflammatory process in atherosclerosis.

Keywords: atherosclerosis, oxidized low-density lipoproteins, antibodies against oxidized low-density lipoproteins, inflammation.

Peripheral atherosclerosis diagnostics by the circulating biomarkers determination

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Abstract

Lower extremities atherosclerosis – severe disabling disease, which leads to ischemia of the extremities. Peripheral atherosclerosis is the main cause of non-traumatic amputations. Due to different clinical features or asymptomatic, the disease is often underdiagnosed at the early stages and the treatment is initiated already in severe defeat when only surgery allows the limb salvage. Currently there is a strong need for specific biomarkers of peripheral atherosclerosis determination. Diagnosis of peripheral atherosclerosis by analyzing blood in the early stages is easier and cheaper than instrumental examination and can help prescribe adequate treatment to prevent severe complications.

Keywords: peripheral atherosclerosis, circulating biomarkers, C-reactive protein, interleukin-6, beta2-microglobulin.

Metabolic syndrome in the Baikal region: ethnic peculiarities of dyslipidemia

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Abstract

Objective. To determine the ethnic peculiarities of dyslipidemia in patients with metabolic syndrome from the Baikal region.

Materials and methods. The study included 254 patients with metabolic syndrome, which were defined by the JIS criteria (2009): 100 women and 154 men aged 36 to 79 years. There were 120 patients of Buryat ethnic group and 134 Russian patients among them.
Results. The most common components of metabolic syndrome in both the Russian and the Buryat ethnic groups were hypertension and abdominal obesity, and more rare component was carbohydrate metabolism disorder. The prevalence of the dyslipidemia was high (83 %), equal among men and women. It was defined that in the Buryat ethnic group the level of low-density lipoprotein cholesterol (LDL-C) was significantly lower and the level of high-density lipoprotein cholesterol (HDL-C) was significantly higher compared to Russian patients.
Conclusion. Severity of lipid profile atherogenic changes (increase of LDL-C and decrease of HDL-C) was significantly more pronounced in Russian patients compare to Buryats. This fact must be considered while planning the treatment of metabolic disorders of Buryat patients.

Keywords: dyslipidemia, metabolic syndrome, Buryat, Russian, population, Baikal region.

The association of genetic risk factors of atherosclerosis with traditional risk factors of atherosclerosis in patients with coronary heart disease living in highlands (at the example of Karachay-Cherkessia

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Abstract
Objective. To study significance of the heteroplasmy of the mitochondrial genome as the risk factor of atherosclerosis and its association with traditional risk factors in patients with coronary heart disease (CHD) living in highlands.
Materials and methods. 112 patients who came to see a doctor to the polyclinic of central regional hospital of Malokarachaevsky region of Karachay-Cherkessia were included in the research. As a result the examined people were divided into 2 groups. The first group included 77 patients with coronary heart disease, 60 men (78 %) and 17 women (22 %). The second group included 35 patients without CHD according to the examination results, 28 men (80 %) and 7 women (20 %). The average age of patients was 61.5±2.2 years in the first group and 54.1±2.8 years in the second. The determination of behavioral risk factors and clinical and laboratory examination were made.
Results. The study allowed to find out that there wasn't any association between mutations of the mitochondrial genome and the serum lipid profile. Smoking also didn't increase the count of mutations. There was not found any association between the heteroplasmy of mitochondrial genome and other traditional risk factors, such as central obesity and diabetes. Arterial hypertension in anamnesis and systolic blood pressure had negative correlation with the level of heteroplasmy of G15059A mutation. The study also detected a negative correlation between the coronary heart disease and G14846A and G13513A mutations presence.
Conclusions. According to our data G14846A and G13513A mutations may have the antiatherogenic features. A negative correlation between the level of heteroplasmy of G15059A

mutation and such atherosclerotic risk factor as arterial hypertension, may also indicate its indirect antiatherogenic influence.

Keywords: mutation, mitochondrial, genome, heteroplasmy, coronary heart disease, risk factors.

The levels of matrix metalloproteinase-2, -9 and soluble ligand CD 40 in patients with coronary heart disease and susceptibility to psychological distress

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Abstract

Objective. To examine the levels of matrix metalloproteinase (MMP)-2, -9 and soluble CD40 ligand (sCD40L) in patients with coronary artery disease with and without personality type D.

Materials and methods. We examined 744 patients with coronary heart disease at the age of 57.5 (51; 63) years prior to bypass surgery for the period from September 1, 2010 to March 1, 2011. From this cohort the concentrations of non-specific markers of subclinical inflammation: MMP-2, -9 and sCD40L were determined in 131 patients. For further study two groups were revealed: Group I (n = 44) – patients with the presence of type D and Group II (n = 87) – patients with no type D. Determining the type of personality was carried out using DS-14 questionnaire. Standard preoperative laboratory and instrumental studies were performed for all patients. Serum levels of MMP-2, -9 and sCD40L were determined by quantitative solid phase enzyme immunoassay.

Results. Data of almost all indicators were comparable between the two groups. MMP-2 concentration was significantly higher in the group with type D (195 ng/ml vs 169 ng/ml, p = 0.037). In the group with no type D the higher concentrations of MMP-9 (62.5 ng/ml vs 49.3 ng/ml, p = 0.028) and sCD40L (6,25 ng/ml versus 4.45 ng/ml, p = 0.006) were revealed. Parameters of lipids were higher in the group with no type D. According to the results of multivariate analysis independent predictors for MMP-2 increase had been smoking (OR 2.92; 95 % CI 1.11–7.73; p = 0.028) and type D personality presence (OR 3.45; 95 % CI 1.39–8.57; p = 0.007); for sCD40L – type 2 diabetes presence (OR 4.95; 95 % CI 1.25–19.61; p = 0.021). The high level of MMP-9 was associated with stroke history presence (RR 6.02; 95 % CI 1.25–29.03; p = 0.024), and in the lesser degree – with unstable angina presence (RR 3.47; 95 % CI, 0.57–21.02; p = 0.17).

Conclusion. The presence of personality type D contributed to higher MMP-2 levels. The patients without type D had higher levels of lipids and increased levels of MMP-9 and sCD40L.

Keywords: type D personality, markers of subclinical inflammation, coronary heart disease.

Optimization of hemostasis indicators under the influence of statin therapy in patients with ischemic heart diseases

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Abstract
Purpose. To evaluate the influence of statin therapy on hemostatic indicators in patients with coronary heart disease.
Methods. 168 patients with ischemic heart disease (mean age 56.7±4.3 years) were included. We evaluated hemostatic parameters (fibrinogen, D-dimer, interval beginning of ADP-induced platelet aggregation) and endothelial function (von Willebrand factor).
Results. The 24 weeks period of simvastatin 40 mg daily, atorvastatin 55 mg daily and rosuvastatin 20 mg daily reduces of von Willebrand factor and fibrinogen levels ($p < 0.05$). Simvastatin had no significant effect on D-dimer concentration while atorvastatin and rosuvastatin therapy resulted in decreasing of this indicator. Rosuvastatin increases interval to the beginning of ADP-induced platelet aggregation ($p < 0.05$) during 24 weeks.
Conclusion. Long term statin therapy reduces the severity of endothelial dysfunction and trombogenic potential of the blood.

Keywords: coagulation, ischemic heart disease, statins.

Effect of different doses of atorvastatin therapy on endothelial progenitor cells and angiogenic factors in patients with ischemic heart disease

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Abstract
Aim. Research and application of endothelial progenitor cells (EPC) is now considered as a promising trend in cardiology and angiology, since it is known that they are actively involved in the vascular endothelium reparation and angiogenesis. Reduction of EPC levels was demonstrated as an independent predictor of cardiovascular morbidity and mortality. The purpose of current research was to assess changes in EPC and angiogenic factors levels during atorvastatin therapy in ischemic heart disease (IHD) patients, and to compare them with lipid profile dynamics.
Materials and methods. The main group included 58 patients with IHD: 26 patients received 10 mg of atorvastatin and 32 patients received 40 mg of atorvastatin daily. Number of EPC (CD34+/CD133+/CD309+ phenotype) was measured by flow cytometry two times – before treatment and 3 months after. Vascular endothelial growth factor (VEGF), C-reactive protein (CRP), monocyte chemoattractant protein-1 (MCP-1), endostatin levels and lipid profile were also measured twice. The control group consisted of 10 healthy volunteers with the same analyzes performed once.
Results. The results showed that EPC levels were 4 times lower, VEGF levels were 52 % higher and endostatin levels were 13 % lower in IHD patients compared to healthy volunteers ($p < 0.05$). Atorvastatin therapy in IHD patients within three months of treatment caused a significant (on average 72 %) increase of EPC levels ($p < 0.05$). EPC gain did not depend on statin dose, but it was higher when initial EPC values were low ($p = 0.01$). The therapy showed reliable levels reduction of VEGF – 11 % ($p < 0.01$), CRP – 26 % ($p < 0.01$), total cholesterol (TC) – 30 % ($p < 0.01$), low-density lipoprotein-cholesterol (LDL-C) – 35 % ($p < 0.01$), triglycerides – 18 % ($p < 0.01$), while endostatin, MCP-1 and high-density lipoprotein-cholesterol levels did not change. Correlations between EPC, TC and LDL-C changes during therapy were revealed: higher

EPC levels gain was associated with higher TC ($p = 0.37$, $r < 0.01$) and LDL-C ($p = 0.41$, $r < 0.01$) levels decrease.
Conclusion. We found a significant increase of EPC levels in IHD patients treated with atorvastatin for 3 month without any significant difference depending on dosage. The EPC increase was higher in patients with smaller initial EPC levels and when higher TC and LDL-C decrease was achieved.
Keywords: endothelial progenitor cells, ischemic heart disease, atorvastatin, angiogenic factors.

About homozygous hyperlipidemias observed in Saint-Petersburg Lipid clinic

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Abstract
The aim was to describe blood plasma lipids profiles and clinical manifestations of atherosclerosis in children with homozygous hyperlipidemias. We observed and followed four children with homozygous hyperlipidemia, measured blood plasma lipids in them and in their parents (when available), and described the clinical consequences of hyperlipidemia in the families of probands. Out of these four cases two were classified as classical autosomal dominant familial hypercholesterolemia. One case was an unique observation because high hypercholesterolemia was observed in a boy despite both parents had normal lipid data. We classified this case as an autosomal recessive hypercholesterolemia. In the paper we also describe a case of severe hypertriglyceridemia in a girl with healthy parents without elevation of blood plasma triglycerides. Genetic analysis was not performed; the diagnosis was established based on clinical parameters and anamnesis data. Nevertheless cases of homozygous hyperlipidemia are very rare, they contribute to a proportion of atherosclerosis cases in adolescents. These cases require special attention, because LDL-apheresis is the only one effective method for treatment of the homozygous.

Keywords: hypercholesterolemia, hypertriglyceridemia, dominant, recessive forms of hyperlipidemia.