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ABSTRACTS

Atherogenic diets and lipid metabolism in different animal species

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Abstract
The development of atherosclerosis in different animals when using a diet-induced models closest to the etiology and pathogenesis of human atherosclerosis. Diet-induced models of atherosclerosis are mainly used for the evaluation of the drugs that inhibit the absorption of cholesterol, promote its degradation, neutralization and excretion. For the simulation of atherosclerosis developed a number of basic diets for different animal groups (diet of the Western type, high-fat diet enriched with cholesterol, high-cholesterol diets, etc.). Most of atherogenic diets for experimental animals include increased amount of fat due to different (mostly animal) sources and cholesterol; some is also used cholic acid or sodium cholat. Foreign manufacturers produced standard atherogenic diets for different animal species, including rodents. Atherogenic diets of Russian production do not exist. The use of a standard atherogenic diets allows you to standardize research.
When planning studies using the model of diet-induced atherosclerosis necessary justification for such important things as choice of animals, the choice of atherogenic diet, the choice of duration of studies, the choice of indicators for the assessment of atherosclerotic changes and their correction. The review presents an analysis of existing atherogenic diets for different animal species and the lipid metabolism they have on these diets (triglyceride, total cholesterol and lipoprotein fraction of cholesterol). As is well seen in the article data, different species react differently to atherogenic diets. The most resistant to the atherogenic diets is genetically no modified mice and rats. Slightly stronger on diets enriched with fat and/or cholesterol, react hamsters. Much more sensitive to the effects of such diets are rabbits, degus and miniature pigs. It was shown that diet-induced model of atherosclerosis can be used in preclinical studies for the evaluation of medicines and biologically active additives to food.
Keywords: atherogenic diets, triglyceride, cholesterol of blood plasma, fractions of cholesterol, pre-clinical studies.

Subfractional profile of apo B-containing lipoproteins in men and women with coronary atherosclerosis treated by statins

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Abstract
Aim. To reveal whether statin therapy affects subfractional distribution of apo B-containing lipoproteins in men and women with documented coronary atherosclerosis.

Materials and methods. The total number of 242 patients (men n= 177; 61 ± 9.0 yrs, and women n= 65; 65.0 ± 9.3 yrs,) who had coronary atherosclerosis verified by angiography were included into the study. Total cohort was split into groups: patients who didn't take statins (ST-) at least 6 months before admission and those who took statins (ST+). LDL subfractional distribution was analyzed using Lipoprint System (Quantimetrix, USA).
Results. ST-men when compared with ST-women in spite on the same LDL C level (3.3 ± 1.0 vs 3.6 ± 1.9 mmol|/l), had lower level of HDL C, apo AI, decreased portion of IDL B, IDL A and increased portion of LDL 2, while no differences in LDL 3 and particles size were detected. More pronounced gender differences in lipid-protein parameters and subfractional distribution were found in ST+ patients: men as compared to women had significantly lower level of LDL C, HDL C, apo AI, apo B, increased portion of VLDL (22.2 ± 4.4 vs 20.1 ± 3.8%), LDL 2 (8.8 ± 3.9 vs 6.5 ± 3.2%), small dense LDL 3 (1.8 ± 1.9 vs 1.3 ± 1.9%) and decreased portion of IDL B (7.4 ± 1.5 vs 8.5 ± 1.7%), and IDL A (7.8 ± 2.1 vs 9.3 ± 3.0%). Gender differences in cholesterol concentration in LDL subfractions were found as well. These differences were associated with lower mean LDL particles size (269 ± 3.7 vs 271 ± 3.9 Å; $p < 0.01$).
Conclusion. Gender differences were found in subfractional distribution of apo B-containing lipoproteins as well as in cholesterol concentration in LDL subfractions. Inspite statin therapy subfractional apo B-containing lipoproteins profile in men with coronary atherosclerosis appeared to be more atherogenic than in women with predominance of VLDL, LDL2 and small dense LDL3.
Keywords: coronary atherosclerosis, apolipoproetein B-containing lipoproteins, subfractional distribution, statins, gender differences.

Association of biomolecules of secretory activity of visceral adipocytes with long-term results of myocardial revascularization in men with coronary atherosclerosison the background of metabolic syndrome

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Abstract
Aim. The study in coronary atherosclerosis (CA) and metabolic syndrome (MS) of blood biomolecules associated with secretory activity of visceral adipocytes, and the search for their associations with long-term 5-year results of coronary artery bypass grafting (CABG).
Material and methods. The study included 123 men 41–79 years with a CA, verified coronary angiography and with stable angina pectoris. Components and signs of MS were evaluated: waist circumference (OT), arterial pressure (SBP, DBP), blood lipids and glucose levels. In blood, the levels of biomolecules associated with the secretory activity of visceral adipocytes (tumor necrosis factor alpha, TNF-alpha, interleukin 6, IL-6, leptin, resistin, adiponectin) were determined by blood enzyme immunoassay. The results of a 5-year course of CA after surgical myocardial revascularization were obtained and 4 groups of men with complicated CA flow were identified (myocardial infarction, MI, cardiovascular death, CVD, repeated surgical myocardial revascularization, unfavorable long-term period in general).
Results. MS as a whole in the group was revealed in 86 men (69.9%) with abdominal obesity and CA. The level of TNF-alpha, was elevated in 47.2% of men, the level of IL-6 in 72.4%, the

level of hBCR in 64.2%, the level of leptin in 47%, the level of resistin 54%, the level of adiponectin was reduced in 22% of cases. In men in the 5-year distant period with developed MI, with a repeated operation and with an unfavorable long-term period in general (MI and/or CVD and/or reoperation), the level of blood leptin was 2.8 times higher before the operation of the CABG ($p< 0.0001$), 1.8-fold ($p< 0.05$), and 1.6-fold ($p< 0.05$), respectively, compared with persons without complications in the long-term period. In men with CVD cases in the long-term period prior to the CABG operation, the blood levels of TNF-alpha, and resistin were 2.8 times higher and 1.6 times, respectively ($p< 0.05$), compared to those without CVD in the distant period. Positive correlations ($p < 0.05$) between the level in the blood of leptin and MI, reoperations and, in general the unfavorable long-term period, as well as between the levels of TNF-alpha, resistin and cases of CVD in the long-term period were found. In multivariate regression analysis, it was found that an elevated blood level of leptin is associated with a relative risk of reoperation in the 5-year period after CABG (OR= 1.261; 95% CI: 0.994–1.599; $p< 0.047$) and the relative risk of a generally unfavorable long-term period (OR= 1.265, 95% CI: 1.016–1.577, $p< 0.036$).

Conclusion. There is an association of elevated leptin levels in the blood with adverse long-term 5-year results of myocardial revascularization in men with coronary atherosclerosis in the background of metabolic syndrome.

Keywords: coronary atherosclerosis, metabolic syndrome, leptin, adiponectin, resistin, TNF-alpha, IL-6.

Carotid intima-media thickness in patients with arterial hypertension among the population of Gornaya Shoriya: relationship with genetic factors

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Abstract

Purpose. We aimed to identify the associations of polymorphisms of ACE, AGT, AGTR1, ADRB1, ADRA2B, MTHFR and NOS3 candidate genes with the increased carotid intima-media thickness (CIMT) in patients with arterial hypertension (AH) among indigenous (the Shors) and non-indigenous population of Gornaya Shoriya.

Material and methods. We performed a clinical and epidemiological study of the compactly settled population in the remote areas of Gornaya Shoria. This region of middle mountains is situated in the south of Western Siberia. We examined 830 subjects [494 subjects – the representatives of indigenous nationality (the Shors), 336 subjects – representatives of non-indigenous nationality (90% among them were the representatives of the European ethnicity)]. AH was diagnosed according to the National Guidelines of the Russian Society of Cardiology/the Russian Medical Society on Arterial Hypertension (2010). The thickness of carotid intima-media in patients with AH was evaluated using ultrasound duplex scanning at Medison Sonoace PICO apparatus (235 subjects among the Shors and 178 subjects among the non-indigenous inhabitants). Polymorphisms of genes ACE (I/D, rs 4340), AGT (c.803T > C,

rs699), AGTR1 (A1166C, rs5186), ADRB1 (c.145A > G, Ser49Gly, rs1801252), ADRA2B (I/D, rs 28365031), MTHFR (c.677C > T, Ala222Val, rs1801133) and NOS3 (VNTR, 4b/4a) were tested using PCR.

Results. The frequency of the increased CIMT in patients with AH was higher in the indigenous ethnic group (78.3%) as compared with the non-indigenous group (69.7%, p= 0.046). A correlation analysis revealed a direct correlation between the levels of systolic and diastolic blood pressure and CIMT (r = 0.4, p= 0.0001 and r= 0.3, p= 0.0001 among the Shors; r= 0.3, p= 0.0001 and r= 0.2, p= 0.0001 among the non-indigenous population, respectively). In the group of the examined subjects with AH and carotid atherosclerosis the frequency of homozygous I/I genotype of ACE gene in the cohort of the Shors was higher, and the frequency of heterozygous I/D genotype, on the contrary, was lower than in the cohort of non-indigenous representatives. In the group of subjects with the indicated pathology the percentage of the carriers of the prognostically favourable I/I genotype of ADRA2B gene among the Shors was lower than among the subjects of non-indigenous ethnos. The similar pattern was also revealed regarding to the prevalence of mutant T/T genotypes of MTHFR gene and 4a/4a of NOS3 gene.

Conclusion. The association of T/C genotype of AGT gene and C/T genotype of MTHFR gene in a superdominant mode of inheritance with carotid atherosclerosis was established in the cohort of the Shors. The risk effect of C/T genotype of MTHFR gene was increasing in female subjects aged 18–64 years and having dyslipidemia. The protective effect was revealed for ADRB1 gene in log-addictive mode of inheritance. In the cohort of non-indigenous ethnos AGT gene in log-addictive mode of inheritance was associated with carotid atherosclerosis. The protective effect was established for I/D genotype of ADRA2B gene in a superdominant mode of inheritance.

Keywords: carotid intima-media thickness, associations of candidate genes, ethnos.

Gender-related differences in patients with obliterating lower extremity arterial disease

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Abstract

Aim: to identify gender-related differences in the prognosis of patients with obliterating atherosclerosis of lower extremity arteries (LEA) in the outpatient setting and to determine factors, associated with fatal outcomes in men and women.

Material and Methods. 453 patients with obliterating atherosclerosis of lower extremity arteries who were examined by interventional cardiologist in the Kemerovo Cardiology Center in the period from 2009 to 2013 were retrospectively reviewed. All patients were assigned to two groups: Group 1 – female patients (n = 93), and Group II – male patients (n = 360).

Results. Women were commonly older than men, and had higher body mass index. Women suffered more often from arterial hypertension and diabetes (p> 0.05). Thus, smokers prevailed among men (p < 0.001). The rate of the major adverse events was assessed in both groups. 5 patients (5.4%) died in Group 1, and 36 patients (10%) – in Group 2 (p = 0.165). 8 (8.6%) women and 23 (6.4%) men had myocardial infarction (MI) and stroke (p> 0.05). 8 male patients (2.2%) underwent amputation (p = 0.146). According to the logistic regression analysis, the independent predictors for adverse events in the group of male patients included the presence of angina pectoris and verified coronary artery disease (p = 0.014 vs p = 0.032), internal carotid

artery stenosis (p = 0.013), LEA stenosis > 50%, p = 0.033), a positive history of amputation (p = 0.004), and chronic renal failure (p = 0.012). Multivariate analysis performed in the group of female patients reported that previous MI and elevated pulmonary artery systolic pressure (PASP) contributed to the increased likelihood of adverse events (p = 0.066 vs p = 0.072).
Conclusion. There were no significant gender-related differences found in the incidence of adverse outcomes within the 3-year follow-up of patients with obliterating atherosclerosis of lower extremity arteries (p> 0.05). The factors associated with adverse events in the group of male patients included the presence of cardiac pathology, renal insufficiency, severe peripheral arterial stenoses, and a positive history of lower extremity amputation of the lower limbs. Thus, the factors contributing to the increased likelihood of major adverse outcomes in the group of female patients were as follows: prior MI and elevated PASP. The results of the study should be taken into account when developing personalized treatment regimen and prevention programs for men and women with obliterating atherosclerosis of lower extremity arteries.
Keywords: obliterating atherosclerosis of lower extremity arteries, gender-related differences.

Study of the microvasculature in patients with acute myocardial infarction in the hospital and ambulatory clinic

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Abstract
The assessment of microcirculation in healthy volunteers and in patients after acute myocardial infarction, depending on the use of thrombolysis. Evaluated the dynamics of the studied parameters after 6 months after myocardial infarction. In patients with acute myocardial infarction had an increased tonus of vessels of microvasculature and impaired response of the microvasculature in response to stimuli (cold test and the test with reactive hyperemia). After 6 months showed persistent positive trend, most clearly evident in the group of patients who underwent thrombolytic therapy.
Keywords. Acute myocardial infarction, microvasculature.

Rare forms of familial hypercholesterolemia revealed in Saint-Petersburg (Russia) and verified by genetic investigation (clinical cases)

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Abstract
Genotypic and phenotypic manifestations of familial hypercholesterolemia are of great variability. We represent two rare clinical cases of familial hypercholesterolemia. A young female with homozygous phenotype (high LDL-C levels, multiple tendon xanthomas and premature coronary and cerebral atherosclerosis). Genetic investigation showed revealed 2

different mutations in the LDL-receptor gene. The second case is due to the mutation in apoB-100 gene that was never seen before in the population of Saint-Petersburg.

Keywords: familial hypercholesterolemia, genotypic and phenotipic manifestations of LDL-receptor gene mutation and mutation of apoB-100, premature atherosclerosis, management of familial hypercholesterolemia.