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Association of uric acid with coronary atherosclerosis in the population of Yakutia

Abstract

Research objective was to estimate the uric acid levels in patients with the verified coronary atherosclerosis and persons without clinical signs of IHD, and also the frequency of the association of hyperuricemia with coronary atherosclerosis depending on ethnic and gender origin on the example of Yakutia population. Results of the survey of men and women at the age of 45-64 years of native and non-native population with the verified coronary atherosclerosis according to selective coronaroangiography, and also of persons without clinical signs of IHD, were analyzed. The results of the research showed that the uric acid levels were significantly higher in patients with the verified coronary atherosclerosis (excepting of women of non-native nationality) in comparison with persons without clinical signs of IHD and higher in representatives of non-native nationality, than in the native population of Yakutia.

Keywords: coronary atherosclerosis, uric acid, native and non-native population of Yakutia.

Introduction. Uric acid's role as risk factor to the development of cardiovascular diseases is confirmed in the majority of researches. So, according to W.J. Fessel during a 10-year follow up of patients with hyperuricemia the 10-fold increase in risk of the development of ischemic heart disease (IHD) and arterial hypertension (AG) [11] was noted. In the 12 years' prospective research Chicago Industry Heart Study the uric acid level was an independent risk factor in the frequency of cardiovascular diseases and mortality of women unlike men of whom this factor was insignificant [7]. In the National Health And Nutrition Epidemiologic Study I (NHANES I) from 1971 to 1992, positive communication between hyperuricemia and cardiovascular events, of men and women was noted. Dependence the uric acid level of on race is revealed: among representatives of Negroid race it was higher, than among Caucasian. Thus the risk of developing of cardiovascular diseases in men of Negroid race increased twice, and in women is more senior than 45 years – by 8 times [10]. The reasons of gender distinctions up to the end aren't studied. There is an opinion that a certain role is played by sexual hormones: at the women accepting preparations of estrogen and progesterone, the uric acid level is much lower, than in women who never accepted them. In the period of postmenopausal the maintenance the uric acid is higher, than before its approach [4]. In the research Atherosclerosis Risk in Communities (ARIC) the interrelation between hyperuricemia and early manifestations of atherosclerosis wasn't received [17]. According to the Progetto Ipertensione

Umbria Monitoraggio Ambulatoriale Study (PIUMA) it was shown that an increase in the uric acid level on 1 mg/dl of patients with AG the frequency of cardiovascular events increased by 10%. A similar effect gives increase the systolic arterial pressure on 10 mm of mercury or the total cholesterol level on 20 mg/dl [16]. In the research Multiple Risk Factor Intervention Trial (MRFIT) it was shown that the hyperuricemia is connected with an increase in risk of development of acute myocardial infarction by 26% [18].

Hyperuricemia in recent years many authors include in metabolic syndrome (MS) components. Thus note hyperuricemia association with hypertriglyceridemia and hypercholesterolemia, hypertrophy of myocardium of the left ventricle, obesity, with degree and weight of AG and with number of cardiovascular complications [1-5; 19; 20]. The uric acid level raises along with an increase in number of the MS components. According to population researches it was shown that the uric acid average level of raised with 4,6 to 5,9 mg/dl in patients with existence of three MS components in comparison with persons without metabolic disorders [9; 12; 15]. Uric acid influences on endothelium, smooth muscle cells and adipocytes, inhibits endothelial NO-synthase, stimulates nicotine-amide-adenin-dinucleotid-phosphate-oxidase and inflammation processes, activates local production of angiotensin II, brakes adipokines. All these processes lead to AG and MS development [6; 13; 14]. Realization of these effects requires penetration urates in cell which mechanism up to the end isn't clear. There is assumption that they can include reaction urates with oxygen or nitrogen with education of free radicals [4]. In patients with AG the hyperuricemia is important marker of renal damage. Only in patients with hyperuricemia increase of vascular renal resistance is noted. There is direct interrelation between the uric acid level and resistance of renal vessels, also with microalbuminuria and the return – with renal blood flow.

Research objective: to estimate the uric acid levels in patients with the verified coronary atherosclerosis and persons without clinical signs of IHD, and also frequency of the association of hyperuricemia with coronary atherosclerosis depending on ethnic and gender origin on the example the inhabitants of Yakutia.

Materials and methods. Results of survey of 396 men and 60 women are included in research at the age of 45-64 years with the verified coronary atherosclerosis according to selective coronaroangiography, being on stationary survey in cardiological branch of Republican hospital №1-National center of medicine of Yakutsk which made the main groups. In forwarding actions to areas of the Republic of Sakha (Yakutia) by results of complex medical survey comparison groups of 212 men and 271 women without clinical signs of IHD at the age of 45-64 years are created. Research period: 2007-2010. For the comparative analysis the surveyed persons were subdivided

into 4 groups: 1 – patients with the verified coronary atherosclerosis, representatives of native nationality of Yakutia (n=217), from them men – 189, middle age 54,34 ± 0,44 years, women – 28, middle age 53,39 ± 1,28 years; 2 – patients with the verified coronary atherosclerosis, representatives of non-native nationality of Yakutia (n=239), from them men – 207, middle age 54,76 ± 0,43 years, women – 32, middle age 55,81 ± 1,01 years; 3 – persons without clinical signs of IHD, representatives of native nationality (n=253), from them men – 108, middle age 51,28 ± 0,57 years, women – 145, middle age 51,19 ± 0,43 years; 4 – persons without clinical signs of IHD, representatives of non-native nationality (n=230), from them men – 104, middle age 51,09 ± 0,52 years, women – 126, middle age 51,37 ± 0,47 years. Yakuts are considered to be representatives of native nationality, non-native nationality – Russians, Ukrainians and Belarusians living in Yakutia constantly. As criteria of exception of research served: anomalies of development of coronary arteries, intact coronary arteries, existence of unstable stenocardia, acute myocardial infarction in the anamnesis till 6 months for groups of patients; in comparison groups – presence of IHD clinical signs and electrocardiogram-signs of the old myocardial infarction; the acquired and congenital heart diseases, cardiomyopathy, worsening of any chronic diseases, age are more younger than 45 years and of 65 years and are more senior for all groups. The characteristic of the investigated persons is presented in table 1.

Table 1

The characteristic of the investigated groups of men and women

Parameter	**Groups of patients with IHD**	**Groups of persons without IHD sings**						
	Native (1) (n=217)		**Non-native (2)** (n=239)		**Native (3)** (n=253)			
	men	**women**	**men**	**women**	**men**	**women**	**men**	**women**
Number of the surved persons, n (%)	189 (87,1)	28 (12,9)	207 (86,6)	32 (13,4)	108 (42,7)	145 (57,3)	104 (45,2)	126 (54,8)
	p_{m-w}=0,000		p_{m-w} =0,000		p_{m-w} =0,000			
Adress, n (%)	City / village							
	76 (40,2)/ 113 (59,8)	10 (35,7)/ 18 (64,3)	91 (44)/ 116 (56)	19 (59,4)/ 13 (40,6)	50 (46,3)/ 58 (53,7)	43 (29,7)/ 102 (70,3)	50 (48,1)/ 54 (51,9)	45 (35,7)/ 81 (64,3)
	p_{c-}	p_{c-}	p_{c-}	p_{c-}	p_{c-}	p_{c-}	p_{c-}	p_{c-}

	$_c$=0,000	$_c$=0,037	$_c$=0,000	$_c$=0,139	$_c$=0,278	$_c$=0,000	$_c$=0,580	$_c$=0,000
	54,22±0,42		54,91±0,39		51,23±0,35			
Middle age, years	54,34±0,44	53,39±1,28	54,76±0,43	55,81±1,01	51,28±0,57	51,19±0,43	51,09±0,52	51,37±0,47
	p_{1-3}=0,000		p_{2-4}=0,000					
BMI, kg/m²	28,64±0,33	28,29±0,74	29,62±0,29	32,97±1,02	26,09±0,41	26,14±0,38	27,92±0,47	27,08±0,42
	p_{1-3}=$_м$0,000-$_ж$0,009		p_{2-4}=$_м$0,001-$_ж$0,000					
TC, mmol/l	6,15±0,07	6,49±0,19	6,92±0,09	6,56±0,13	4,74±0,07	4,75±0,07	5,16±0,09	5.34±0,08
	p_{1-3}=0,000		p_{2-4}=0,000; p_{1-2}=$_м$0,001					
TG, mmol/l	1,84±0,07	1,81±0,15	2,20±0,09	2,29±0,23	0,99±0,05	0,99±0,03	1,28±0,07	1,14±0,06
	p_{1-3}=0,000		p_{2-4}=0,000; p_{1-2}=$_м$0,003					
HDL, mmol/l	1,06±0,04	1,52±0,13	1,14±0,06	1,00±0,05	1,45±0,04	1,60±0,04	1,47±0,03	1,68±0,04
	p_{1-3}=$_m$0,000; p_{1-2}=$_w$0,001		p_{2-4}=0,000					
Glucose, mmol/l	5,39±0,09	5,07±0,20	5,50±0,10	6,22±0,45	4,22±0,05	4,49±0,11	5,22±0,07	4,92±0,07
	p_{1-3}=0,000		p_{2-4}=$_m$0,059-$_w$0,000					
Diabetes millitus, n (%)	29 (15,3)	5 (17,9)	32 (15,5)	12 (37,5)	0	2 (1,4)	1 (1)	0
	p_{1-3}=0,000		p_{2-4}=0,000					
AG, n (%)	155 (82)	19 (67,9)	166 (80,2)	29 (90,6)	38 (35,2)	50 (34,5)	33 (31,7)	32 (25,4)
	p_{1-3}=0,000		p_{2-4}=0,000					
Smoking, n (%)	84 (44,4)	8 (28,6)	120 (58)	3 (9,4)	61 (56,5)	51 (35,2)	46 (44,2)	33 (26,2)
			p_{2-4}=$_m$0,022; p_{1-2}=$_m$0,007		p_{1-3}=$_m$0,046			
Family history of IHD, n (%)	94 (49,7)	15 (53,6)	77 (37,2)	21 (65,6)	34 (31,5)	88 (60,7)	17 (16,3)	42 (33,3)
	p_{1-3}=$_m$0,002; p_{1-2}=$_m$0,012		p_{2-4}=0,000		p_{3-4}=$_m$0,010-$_w$0,000			

Survey was spent by standard techniques and included following obligatory sections: standard poll under Rose's questionnaire (for comparison groups) and the questionnaire developed for estimation of objective condition; triple measurement of arterial pressure; anthropometrical survey with measurement of growth, weight and calculation of body mass index (BMI) (BMI = weight (kg)

/ growth (m^2)); electrocardiogram registration in rest; selective coronaroangiography (for patient groups); blood sampling from elbow vein in the morning on empty stomach for revealing of purine (uric acid), lipid (total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL)) and carbohydrate (blood glucose) metabolism disorders. All researches are executed from the informed consent of examinees according to ethical standards of the Helsinki declaration (2000). Estimation of results spent on the standard classifications.

Statistical processing of the received data was held by means of package of computer programs SPSS (version 13). Results are presented in the form of M ± m, where M – average arithmetic, m – standard error of average. The importance of distinctions was estimated with t-Student criterion, χ2-Pearson. Distinctions were considered statistically significant at $p < 0,05$.

Results and discussion. The comparative analysis showed that the uric acid average levels were significantly higher in patients with the verified coronary atherosclerosis (excepting of women of non-native nationality) in comparison with persons without clinical signs of IHD (native: men – 336,18 ± 9,95 vs 299,08 ± 9,33, p=0,001; women – 318,61 ± 14,31 vs 255,64 ± 4,90, p=0,000; non-native: men – 368,79 ± 9,46 vs 273,65 ± 9,31, p=0,000 accordingly) (tab. 2). Ethnic differences were characterized by elevated the uric acid levels among not indigenous people in comparison with aboriginals in group of patients in men (368,79 ± 9,46 vs 336,18 ± 9,95, p=0,013 accordingly) and in group of comparison in women (303,31 ± 5,76 vs 255,64 ± 4,90, p=0,000 accordingly). The significant gender differences which are characterizing in group of patients among not indigenous people by increase the uric acid level in men in comparison with women (368,79 ± 9,46 vs 320,93 ± 18,88, p=0,004 accordingly) are received. In group of comparison in native men the uric acid level in comparison with women (299,08 ± 9,33 vs 255,64 ± 4,90, p=0,000 accordingly) was higher. Among not indigenous people in group of comparison in women the uric acid level (303,31 ± 5,76 vs 273,65 ± 9,31, p=0,006 accordingly), than in men was higher. The uric acid level was higher of non-native urban residents without IHD, as men (291,80 ± 10,49 vs 255,50 ± 15,07, p=0,043 accordingly), and women (319,62 ± 10,14 vs 294,25 ± 6,81, p=0,022 accordingly) in comparison with country people. Uric acid's role of the development of cardiovascular diseases and their complications is so far disputable and remains in the center of close attention of researchers [4; 9; 11]. According to the research executed in Korea, shown that uric acid level is associated with MS and coronary atherosclerosis [8]. The high uric acid levels in patients with coronary atherosclerosis according to our research, is possible, connected and that more than 80% of patients suffered arterial hypertension and about 40% had obesity at which function of renal is broken. Results of the research shown that among inhabitants of Yakutia the hyperuricemia has significant positive

correlation with coronary atherosclerosis (r=0,345, p < 0,01), lipid (r=0,320, p < 0,01) and carbohydrate (r=0,146, p < 0,01) metabolism disorders, arterial hypertension (r=0,241, p < 0,01) and obesity (r=0,185, p < 0,01).

Table 2

The comparative characteristic the uric acid levels in the investigated groups of men and women, M ± m

Indicator	Sex	Adress	1 Group with IHD native	2 Group with IHD non-native	3 Group without IHD native	4 Group without IHD non-native
Uric acid	men	city	349,36±15,37	352,05±13,29	299,26±15,87	291,80±10,49
		village	324,55±12,83	383,79±13,17	298,90±9,99	255,50±15,07
		total	**336,18±9,95**	**368,79±9,46**	**299,08±9,33**	**273,65±9,31**
		p	$p_{1-3}=0,001$	$p_{2-4}=0,000$ $p_{1-2}=0,013$ $p_{м-ж}=0,004$	$p_{м-ж}=0,000$	$p_{г-с}=0,043$
	women	city	328,00±16,32	305,88±27,18	268,05±9,73	319,62±10,14
		village	313,39±20,56	342,82±24,14	250,41±5,59	294,25±6,81
		total	**318,61±14,31**	**320,93±18,88**	**255,64±4,90**	**303,31±5,76**
		p	$p_{1-3}=0,000$			$p_{3-4}=0,000$ $p_{м-ж}=0,006$ $p_{г-с}=0,022$

Conclusion. Results of the research shown that hyperuricemia associated with coronary atherosclerosis, AG, obesity, lipid and carbohydrate metabolism disorders among population of Yakutia. Uric acid level is higher in representatives of non-native nationality in comparison with aboriginals of Yakutia.

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