YAKUT MEDICAL JOURNAL 2(46)2014

*LPL*rs320 Lipoprotein Lipase Gene Polymorphism: Comparative Characteristics in Different Populations

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ABSTRACT

Gene *LPL*, encoding enzyme lipoprotein lipase, is the one of the most important genes associated with lipid disorders and the risk of metabolic syndrome. Earlier *LPL* rs320 gene polymorphism has been reported to be significantly associated with type 2 diabetes in the Yakut population. The **aim** of this study was to compare *LPL* rs320 SNP (G/T) allele frequency in different world populations, including the Yakuts and analyze blood glucose level, systolic blood pressure and body mass index in patients with type 2 diabetes and healthy individuals of Yakut ethnic group, depending on the genotype rs320 LPL. So the paper presents a comparison of allele frequencies SNP (G / T) gene *LPL* rs320, which contributes to the development of a predisposition to type 2 diabetes mellitus in the Yakut population, with distribution of allelic variants of this SNP in other world populations. Also the authors studied the blood glucose level, systolic blood pressure and body mass index, depending on the variant genotype rs320 *LPL* in patients with type 2 diabetes and healthy individuals of the Yakut ethnic group. The obtained during the study data reveal that in the Yakut population allele G variant rs320 *LPL* is most prevalent, with which a reduced risk of dyslipidemia and metabolic syndrome under the conditions of traditional nutrition type in the North with a high content of proteins and lipids is associated.

Keywords: gene *LPL* rs320, lipoprotein lipase, metabolic syndrome, type 2 diabetes mellitus, genetic predisposition.

INTRODUCTION

Lifestyle of modern man has undergone dramatic changes over the last decade. It causes high prevalence of diseases associated with metabolic disorders such as metabolic syndrome and type 2 diabetes mellitus (T2DM). In understanding the molecular mechanisms that lead to disruption of metabolic processes that evolved millennia of human adaptation to the environment, genetic studies play an important role. Yakutia is distinguished by its extreme climatic conditions, peculiar traditional lifestyle and diet of the indigenous population. Study of gene polymorphism in comparison with that of other populations living in different conditions will contribute to a better understanding of changes in the metabolism of modern human.

One of the most important genes associated with lipid disorders and the risk of metabolic syndrome, is the gene *LPL*, encoding a key fat metabolism enzyme - lipoprotein lipase. Previously, we found that genetic polymorphism *LPL* rs320 is a major contributor to susceptibility to type 2 diabetes in the Yakut population [1]. *LPL* gene is located on 8 chromosome - 8p22. Nowadays, more than 100 mutations were identified, many of which were associated with a reduction in the enzymatic activity of *LPL* [11]. Gene polymorphism is associated with dyslipidemia: high triglycerides, low HDL, and high levels of blood pressure (BP) [5, 7, 8, 10]. The connection between gene and insulin resistance and type 2 diabetes is marked [13].

The paper presents the comparative frequency of allelic variants of the gene *LPL* rs320 in different populations, including the Yakut one. The data on the effect of genotypes on blood glucose level, systolic blood pressure and body mass index in the Yakut population are reported.

MATERIALS AND METHODS

The study included 344 people - the indigenous inhabitants of the Central Yakutia, 194 were patients with T2DM and 150 individuals who were not in relationship with patients and did not suffer from T2DM. Body mass index (BMI) of patients was calculated using the formula BMI = body weight (kg) / height (m^2). Blood pressure was determined by the double measuring with mercury sphygmomanometer on the right arm in a sitting position. Measurement of capillary blood glucose was performed using glucometer ACCU-CHEK, ADVANTAGE, and SOFTCLIX (trademarks of a Member of the Roche Group).

DNA of patients was isolated from white blood cells by the method of Wizard ® Genomic (Promega, Madisan, WI). Genotyping was performed at the Institute of Neurological Disorders and Strokes of Health Institutes, USA (Bethesda) by the procedure described in detail in a previous publication [1].

All study participants gave written voluntary informed consent to participate in the study. The study protocol is approved by the local Committee on Biomedical Ethics YSC CMP SB RAMS (protocol number 5, June 21, 2006).

In our study, quantitative measures of blood glucose, blood pressure and BMI did not have a normal distribution, and were described as median and interquartile range (Me (25-75 %)). Comparison of allele frequency of *LPL* rs320 in different populations was carried out by comparing the 95% confidence interval (95% CI). *LPL* gene variants association with glucose and blood pressure levels was detected using the nonparametric Kruskal -Wallis criteria.

RESULTS AND DISCUSSION

In European populations, the minor allele of *LPL* SNP (G / T) rs320 is G allele; its frequency is estimated from 24 to 32 % [3, 9, 12]. With this gene allele high enzyme activity is associated. The prevalence data of genotypes and alleles of this gene in Asian, Indian and Arab populations do not differ from European ones (Table 1) [2, 4, 6, 12, 13]. The highest frequency of G allele among healthy individuals is revealed in Saudi Arabia. [4]

Table 1

Minor allele frequency *LPL* rs320 in different world populations

Population	Minor allele frequency (G), %	Number of patients	Reference	95% CI minor allele frequency, %
China	19.7	654	[13]	17.6-21.9
Canada	24	334	[9]	21-27
India	24.6	1015	[2]	
China	25	56	[6]	
Spain	32	1029	[3]	30-34
Saudi Arabia	37.6	65	[4]	29.5-46.6
European race (19 studies)	29.1	3540	[12]	
Asian race (4 studies)	28.9	479	[12]	

For comparison of the frequency of the minor allele polymorphism *LPL* rs320 we calculated 95% CI of the minor allele share in some populations. The frequency of the minor allele G in the Chinese population in one of studies is 19.7%, in the Spanish Mediterranean population 32, Saudi Arabia 37. 6 %. In our studies of the Yakut population frequency of this allele in patients with type 2 diabetes is 21 %, while in the control group 54% (Table 2). Comparison of the 95 % CI in healthy individuals shows that the Yakut population differs in allelic gene frequency *LPL* (rs 320) from other world populations.

Table 2

Allele and genotype frequency *LPL* gene rs320 in type 2 diabetes mellitus patients and healthy individuals in Yakut population

	Allele				Genotype					
	G		T		GG		GT		TT	
	%	95%CI	%	95%CI	n	%	n	%	n	%
Healthy	53.8	49.6-57.9	46.2	42.0-50.4	117	42.4	63	22.8	96	34.8
T2DM patients	21.1	17.3-25.3	78.9	74.6-82.7	4	1.9	78	38.2	122	59.8

According to the literature, pathological allele polymorphism of *LPL* rs320 gene is T allele, with which high triglyceride level and low HDL are associated (2, 3, 5, 8).

To assess the impact of *LPL* gene variants in the Yakut population to the level of blood glucose, systolic blood pressure (SBP) and BMI analysis of these indicators depending on the genotype of SNP (G / T) rs320. The results show statistically significant differences in individuals with different genotypes in the level of glucose, SBP and BMI (Table 3). However, consideration of the indicators within the group of patients with type 2 diabetes and healthy subjects did not reveal significant differences (Tables 4, 5). Differences in the level of glucose throughout the sample due to the fact that initially selected for the study were patients diagnosed with type 2 diabetes , i.e. high levels of blood glucose. Nevertheless, in the control group as a trend due TT genotype with higher levels of glucose, although not statistically significant (Table 5).

BMI is also associated with genotype *LPL* rs320 in a joint sample of patients and healthy subjects (Table 3). The highest BMI was found in TT genotype in patients with type 2 diabetes (Table 4).

Table 3

Glucose level, SBP and BMI according to *LPL* rs320 genotypes in sample including type 2 diabetes patients and healthy individuals of Yakut population

LPL rs320 genotype	Glucose, mmol/l		SBP, mmHg.		BMI, kg/m^2	
	Me (25-75%)	n	Me (25-75%)	n	Me (25-75%)	n
GG	4.95 (4.55-5.6)	52	140 (130-150)	50	25.13 (23.1-26.5)	48
GT	9.3 (5.3-13.3)	85	147.5 (135-160)	96	26.37 (25.0-29.3)	84
TT	8.4 (5.6-14)	129	150 (140-170)	127	27.08 (24.5-30.2)	96
p	**0.0000**		**0.0005**		**0.0014**	

Table 4

Glucose level, SBP and BMI according to *LPL* rs320 genotype in type 2 diabetes patients of Yakut population

LPL rs320 genotype	Glucose, mmol/l		SBP, mmHg.		BMI, kg/m^2	
	Me (25-75%)	n	Me (25-75%)	n	Me (25-75%)	n
GG	15.5 (10.1-18.5)	4	150 (135-170)	4	25.2 (23.7-30.0)	3
GT	12.2 (9.1-14.8)	56	150 (130-165)	96	26.7 (25.7-29.9)	53
TT	12.1 (7.4-15.0)	95	160 (140-170)	109	27.8 (25.5-32.0)	75
p	0.48		0.41		0.49	

Table 5

Glucose level, SBP and BMI according to *LPL* rs320 genotypes in healthy individuals of Yakut population

LPL rs320 genotype	Glucose, mmol/l		SBP, mmHg.		BMI, kg/m^2	
	Me (25-75%)	n	Me (25-75%)	n	Me (25-75%)	n
GG	4.8 (4.4-5.4)	48	140 (130-150)	46	25.1 (23.0-26.4)	45
GT	5.0 (4.2-5.4)	29	140 (140-150)	29	25.6 (22.9-27.4)	31
TT	5.2 (4.8-5.7)	34	140 (130-150)	18	23.7 (22.9-26.1)	21
p	0.07		0.37		0.47	

CONCLUSION

The data testify that in the Yakut population with the highest incidence G allele variant rs320 *LPL* (54%) occurs, with which a reduced risk of dyslipidemia under the conditions of traditional nutrition type in the North with a high content of proteins and lipids is associated.

With the T allele rs320 *LPL* gene the development of predisposition to overweight is connected, that leads to the development of metabolic syndrome and type 2 diabetes mellitus. For a deeper understanding of the impact on the metabolic processes of the gene and its role in the pathogenesis of type 2 diabetes further study of a representative sample of healthy individuals is required.

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