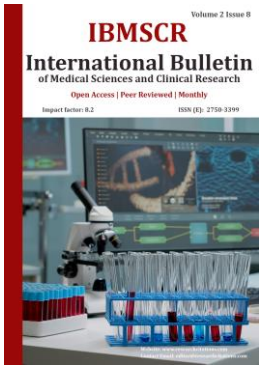

EVALUATION OF THE ROLE OF ADRB 2 IN THE PATHOGENESIS OF SYNTROPIA MYOCARDIAL INFARCTION AND METABOLIC SYNDROME

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Objective: To study the genetic risk factors for MS formation by studying mutations of the Arg16/Gly and Gln27Glu polymorphisms in ADRBthe ADRB 2 gene..

Materials and methods: The material for molecular genetic research was peripheral blood of 64 patients with MS+MI (the main group) and 155 conditionally healthy donors (the control group).

Results: Detection of an unfavorable Glu/Glu genotype of the Gln27Glu polymorphism in ADRBthe ADRB 2 gene increases the risk of MS+MI formation by 3.9 times (15.6% vs. 4.5% at $\chi 2<7.8$, p=0.01, 95%CI:1.5-10.2, OR=3.9).

Conclusion: Thus, the study shows the prognostic significance of the minor-type Glu allele and the associated mutant Glu/Glu genotype not only in terms of the development of MS, but also as an additional genetic marker of the nature of MI in patients with MS.

Key words: Metabolic syndrome, myocardial infarction, Gln-27Glu genetic polymorphism of the ADRB2 gene,genotype, arterial hypertension, lipid spectrum.

Relevance. Despite the achievements of modern medicine, high mortality from cardiovascular diseases (CVD) persists all over the world [1,3,8]. One of the reasons for this is the metabolic syndrome (MS), which has not lost its relevance to date and continues to be one of the main causes of high disability among the working-age population. According to the conducted studies, it is predicted that the incidence of MS will increase 2-fold over the next 25 years [2,4,7]. According to experts, most people "spend an average of 10 years of their life in a state of illness" [5]. At the same time, the presence of a metabolic syndrome is associated with a high risk of developing comorbid diseases. According to literature data, patients with MS develop cardiovascular diseases 3 times more frequently, are more severe, and are more complicated by myocardial infarction than those without metabolic syndrome [6,9,10]. In this regard, early diagnosis, treatment and prevention of the risk of developing metabolic syndrome and myocardial infarction remains one of the most urgent medical problems.

Purpose of research. To study the genetic risk factors for MS formation by studying mutations of the Arg16/Gly and Gln27Glu polymorphisms in ADRBthe ADRB 2 gene..

Materials and methods of research. The material for the molecular genetic study was peripheral blood from 64 patients with MS+MI (the main group) and 155 conditionally healthy donors (the control group). Genomic DNA samples, both independently isolated and stored in the DNA bank of the RSNPMC of Hematology of the Ministry of Health of the Republic of Uzbekistan, were used as the material for the control sample. In groupse of

patients with MS+MI, 64/45 (70.3%) were male, and 64/19(29.7%)were female.- female. In the main study group, the median age wasabout 60.3±1.2 years. The average age of healthy individuals in the control group was 52.3±3.9 years. The age and gender composition of the study and control groups were comparable.

Testing of the Arg16/Gly and Gln27Glu polymorphisms in the ADRB2 gene was2 performed on a Rotor-Gene Q device (Quagen, Germany), using a commercial test kit of Syntol LLC (Russia). Statistical processing of the results was performed using the standard OpenEpi V application software package. V9.2

Results and discussion. In patients of group 1 with MS+MI and the control group, there were no statistically significant differences in the frequency of occurrence of the wild Arg allele (69.5% vs. 69.7%) and the unfavorable Gly allele (30.5% vs. 30.3%) (at $\chi2<0.0$, $p>0.9$, 95%CI:0.6-1.55, OR=1.0 and $\chi2<0.0$, $p>0.9$, 95%CI:0.64-1.58, OR=1.1). In the group of patients with MS+MI, a relative increase in the favorable Arg/Arg genotype was detectedthan in the control group, but this difference was not significantly significant (51.6% vs. 50.3% with $\chi2=0.0$; P=0.9, 95%CI:0.59-1.88, OR=1.1). There were no statistically significant differences in the frequency of occurrence of other genotypes (Arg/Gly-35.9% vs. 38.7% and Gly/Gly-12.5% vs. 11.0%) between the compared groups (MS+MI and the control group) ($\chi2<3.84$, $p>0.05$) (see Table 1).

Table 1

Carriage of alleles and genotypes of the Arg16/Gly polymorphism in the ADRB2 gene in the group of patients with MS+MI and in the control groupe

Alleles and genotypes	Number of examined alleles and genotypes				χ2	p	OR	95%CI
	MS + MI		Control group					
	n	%	n	%				
Arg	89	69,5	216	69,7	0,0	0,99	1,0	0,63 - 1,55
Gly	39	30,5	94	30,3	0,0	0,99	1,0	0,64 - 1,58
Arg/Arg	33	51,6	78	50,3	0,0	0,90	1,1	0,59 - 1,88
Arg/Gly	23	35,9	60	38,7	0,1	0,80	0,9	0,49 - 1,63
Gly/Gly	8	12,5	17	11,0	0,1	0,80	1,2	0,47 - 2,84

According to the comparative analysis data, all allelic and genotypic frequencies of the Gln27-Glu polymorphism in the ADRB2 geneADRB, except for the heterozygous Gln/Glu genotype (45.3% vs. 39.4% at $\chi2<0.7$, $p>0.5$, 95% CI:071-2.3,OR=1.3), statistically significantly differ in the MS groups+IM compared to the control group. The revealed trends of low detection values of the prevalence of the Gln/Glu heterozygous genotype полиморфизма of the Gln27Glu polymorphism in ADRBthe ADRB 2 gene were confirmed by the analysis of the odds ratio (OR=1.3) development of MS+MI (see Table 2).

The OR value Gluof the minor-type Glu allele (38.3% vs. 24.2%) of the Gln27Glu polymorphism in ADRBthe ADRB 2 gene was 1.9 (at $\chi2=8.9$, p=0.01, 95% CI:1.25-3.01), which characterizes Gluthe minor-type Glu allele as risky and the presence of a mutant Glu allele increases the risk of MS+IM increased by 1.9 times, while the Gln major allele (61.7% vs. 75.8% at $\chi2<8.9$, p=0.01, 95%CI:0.33–0.8, OR=0.5) this polymorphism can be considered as an insignificant and / or protective marker in the development of MS+MI compared to the control sample (see Table 2).

Further, we analyze the obtained low threshold values of OR=0.5 (95%CI:0.28-0.9) at χ2=5.3; p=0.03, may indicate a high statistical reliability of the obtained values, as evidence of the protective effect of the favorable Gln/Gln genotype полиморфизма of the Gln27Glu polymorphism in ADRBthe ADRB 2 gene against the development of MS+MI, which is one of the indicators of the positive quality of the body's protective systems, closely related to the indicators of the somatic status of the examined patients (see Table 2).

Table 2

Carriage of alleles and genotypes of the Gln27Glu polymorphism in ADRBthe ADRB 2 gene in the group of patients with MS+MI and in the control groupe

Alleles and genotypes	Number of examined alleles and genotypes				χ2	p	OR	95%CI
	MS + MI		Control group					
	n	%	N	%				
Gln	79	61,7	235	75,8	8,9	0,01	0,5	0,33 - 0,8
Glu	49	38,3	75	24,2	8,9	0,01	1,9	1,25 - 3,01
Gln/Gln	25	39,1	87	56,1	5,3	0,03	0,5	0,28 - 0,9
Gln/Glu	29	45,3	61	39,4	0,7	0,50	1,3	0,71 - 2,3
Glu/Glu	10	15,6	7	4,5	7,8	0,01	3,9	1,5 - 10,2

An unfavorable genotypic variant of Glu/Glu of this polymorphism can be one of the main causes of MS and make a significant and significant contribution to the development of a genetic predisposition to the risk of developing MS+MI and the clinical phenotype of this disease. Detection of an unfavorable Glu/Glu genotype of the Gln27Glu polymorphism in the ADRB2 gene ADRB increases the risk of MS+MI formation by 3.9 times (15.6% vs. 4.5% at χ2<7.8, p=0.01, 95%CI:1.5-10.2, OR=3.9).

Conclusion. Thus, analysis of the Gln-27Glu polymorphism genetic marker Glu in the ADRB2 gene didnot reveal significant differences in the Gln/Glu genotype. However, we have shown the prognostic significance of the minor-type Glu allele and the associated Glu/Glu mutant genotype not only in terms of the development of MS, but also as an additional genetic marker of the nature of MI in patients with MS.

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