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TO STUDY THE INFLUENCE OF THE IL-1β 3953 C/T GENE ON THE CLINICAL COURSE OF UNSTABLE ANGINA IN YOUNG MEN DEPENDING ON THE CYTOKINE STATUS

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ANNOTATION

In the atherosclerotic process, cytokines are the main marker of inflammation; imbalance between them contributes to the early progression of unstable angina pectoris and leads to the development of acute cardiovascular complications. For this reason, the study of the polymorphic structure of the cytokine network, deciphering the mechanisms of regulation of the functional activity of cells of the immune system and genetic control of the immune response will help researchers in the development of criteria for the susceptibility and resistance of a person to the development of pathological conditions.

Keywords: IHD, cytokine, IL-1β C / T 3953 gene, genotype.

Introduction

Coronary heart disease (CHD), despite significant progress in solving the issues of prognosis, therapy and prevention of this disease, is still one of the urgent problems of modern cardiology [1,3]. In the practice of cardiologists, unstable variants of angina pectoris (UAS) in men at a young age were quite rare, but in recent decades there has been a steady increase in the frequency of its occurrence, since this is an important

socio-economic problem due to early disability and early mortality [2, 5.12]. The wide prevalence and great social significance of coronary artery disease necessitates the timely and most reliable diagnosis of this disease.

Under the conditions of the observed rejuvenation of the age of onset of NVS in men, the main behavioral risk factors (smoking, malnutrition, physical inactivity, intense and harmful working conditions, stress) make a significant contribution, and more and more facts have recently accumulated indicating the importance of inflammatory processes in the vascular wall as a factor development and destabilization of the atherosclerotic process and the associated earlier and frequent development of cardiovascular diseases and their complications [4,6,15].

In the atherosclerotic process, cytokines are the main marker of inflammation, imbalance between them is manifested by an increase in the level of pro-inflammatory interleukins (interleukin-1-β (IL-1β), IL-6, tumor necrosis factor-α (TNF-α)) and a decrease in the level of anti-inflammatory interleukins (IL4, IL-8 and IL-10) [8,10,14]. In particular, hyperproduction of pro-inflammatory cytokines IL-1β, IL-6, TNF-α contributes to the early progression of HCV and leads to the development of acute cardiovascular complications [7,9,13].

One of the important non-modifiable risk factors for the early development of NVS is hereditary predisposition. The relationship of non-modifiable genetic risk factors with a predisposition to the development of NVS is found in certain groups of patients who are exposed to additional unfavorable external risk factors [8,11]. In this regard, an active preventive effect on diseases modified by risk factors in men at a young age prevents the implementation of the impact of unfavorable genetic risk factors.

The study of the relationship between modifiable and non-modifiable, in particular, molecular genetic markers that affect the destabilization and progression of cardiovascular pathology in young men, can make it possible to prevent the development of coronary artery disease in carriers genetically predisposed to the progression of HCV [8,15]. Considering all of the above factors, it will be possible to prevent the disease and take measures for the early prevention of NVS, or at least postpone the timing of its occurrence, which in turn will help improve the severity of the clinical course of the disease in men at a young age.

Purpose of the Study: to study the influence of the IL-1β 3953 C/T gene in the development of unstable angina pectoris in men at a young age, depending on the parameters of the cytokine IL-1β.

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Material and Methods of Research

The object of the study were 130 patients with NVS hospitalized in the departments of somatic resuscitation, emergency therapy No. 1 and 2 of the Samarkand branch of the Republican Scientific Center for Emergency Medical Care in the period 2018-2020. Depending on age, the patients were divided into 2 groups. The 1st group included 70 patients at a young age (from 18 to 44 years). The 2nd group included 60 elderly patients (from 60 to 74 years old). The study used general clinical, genetic and statistical studies.

Results of the Study

In our study, we assessed the genetic polymorphism of the IL-1β gene at position -3953 C/T (rs1143634) in patients with NVS to determine the predictors of the prognosis for the development of adverse outcomes. In this regard, we studied the distribution of the frequencies of alleles and genotypes of the polymorphic variant -3953 C/T (rs1143634) of the IL-1β gene in patients with HCV and healthy individuals of Uzbek nationality. Genotyping of the polymorphic locus of the IL-1β gene (-3953 C/T) rs1143634 was performed in 70 patients with HCV at a young age and 60 patients with HCV at an elderly age of Uzbek nationality.

The T allele is 10.4% more common among patients with NVS in the elderly than among patients with NVS of young age. The C allele, in contrast to the T allele, is more common in patients with NVS at a young age compared to patients with NVS in the elderly and also accounts for 10.4% (χ2=2.84; p=0.09) (Table 1). one).

Table 1 Frequency distribution of alleles 3953 C/T (rs1143634) of the IL-1β gene in patients with NVS at a young and old age

Polymorphism	Alleles	Frequency (%)		χ2	P	OR (95%CI)	RR (95%CI)
		Patients with NVS at a young age (n=70)	Patients with NVS in old age (n=60)				
IL-1β 3953 C/T rs1143634	C	80 (57,1%)	56 (46,7%)	2.84	0.09	1,5238 (0,933-2,4888)	1,2535 (0,9632-1,6312)
	T	60 (42,9%)	64 (53,3%)				

The homozygous T/T variant at position -3953 of the IL-1β gene was 4.3% more common among patients with NVS in the elderly compared to patients with NVS at a young age (χ2=2.53; p=0.11), the homozygous C/C variant is 25.3% less and the heterozygous C/T variant is 29.6% more (χ2=13.07; p=0.0003), (Table 2).

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Table 2 Frequency distribution of the polymorphic locus 3953 C/T (rs1143634) of the IL-1β gene in young and elderly patients with NVS

Polymorphism	Genotypes	Patients with NVS at a young age (n=70)	Patients with NVS in old age (n=60)	χ2	p	OR (95%CI)	RR (95%CI)
IL-1β 3953 C/T rs1143634	C/C	27 (38,8%)	6 (10%)	13,07	0,0003	5,1923 (2,0471-13,1697)	2.6515 (1,3996-5,0233)
	C/T	26 (37,1%)	40 (66,7%)				
	T/T	17 (24,3%)	14 (23,3%)	2,53	0,11	2,3824 (0,8082-7,0224)	1.8103 (0,8577-3,8213)

When studying the relationship of some cytokines with the polymorphic locus -3953 C/T (rs1143634) of the IL-1β gene, it was found that patients who had heterozygous C/T and homozygous T/T genotypes of the IL-1β 3953 C/T (rs1143634) gene had 6 ,6 and 13 pg/ml higher concentrations of IL-1β compared with the homozygous C/C genotype (p1<0.0001*, p2<0.0001*), (Table 3).

Table 3 The level of concentration of the pro-inflammatory cytokine IL-1β depending on the polymorphism of the locus -- 3953C>T (rs1143634) of the IL-1β gene in patients with NVS at a young and old age

Indicators IL-1β concentrations (pg/ml)	IL-1β gene genotype T/C 3953			P-value
	C/C	C/T	T/T	
	1	2	3	
1st group	63,4±5,86	70,2±6,2	79,4±7,2	1vs2: <0,0001*; 1vs3: <0,0001*
2nd group	73,7±1,6	82,2±1,39	91,8±1,29	1vs2: <0,0005*; 1vs3: <0,0001*

Conclusions

Thus, according to the data of our study, it was found that among patients with NVS in the age aspect, it was found that the T allele of the IL-1β -3953 C/T gene (rs1143634) is 10.4% more common in elderly patients compared to with young patients. When analyzing the relationship of patients in young and old age with the C/T and T/T genotypes of the IL-1β 3953 C/T gene (rs1143634) and pro-inflammatory IL-1β, it was found that the rates of pro-inflammatory IL-1β were higher compared to patients with C/C genotype. This shows that patients with C/T and T/T genotypes are more prone

to cytokine imbalance and atherosclerotic changes, which in turn worsens the clinical course of the underlying disease.

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