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Features of Gene Polymorphism Il10 G-1082a (Rs3024491) in Patients with Gastric and Duenal Ulcer in Uzbekistan.

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Abstract: In this study, we assessed the degree of participation of the rs3024491 polymorphism of the IL-10 gene in the development of gastric ulcer and duodenal ulcer. Analysis of the results showed that both in the main group of patients and in subgroups of patients with GU and DU, the frequency of occurrence of allelic and genotypic variants of the rs3024491 polymorphism of the IL10 gene (G-1082A) is characterized by the absence of significant statistical differences in comparison with those in the control group, which indicates the absence of its association with the development of GU and DU.

Keywords: pathogenetic mechanisms, proinflammatory cytokine, polymorphism, gastric carcinoma, gastric ulcer.

Introduction

In recent years, significant achievements and progress in modern medicine is largely due to the widespread use of molecular genetic research methods that allowed the disclosure of a completely new data on the genetic basis of diseases, in particular, and, peptic ulcer of the stomach (gastric ulcer) and duodenum (PU) [4]. In this regard, today it is known that the pathogenetic mechanisms of the development of GU and DU are not only the pathogenic effect of Helicobacter Pylori (HbP) [7], but also the individual characteristics of the organism's predisposition, depending on the activity of a number of genes [4]. Results plural study first prove the existence of a connected and between the genes of proinflammatory cytokine s and development of GU and DU [11]. In this regard, first of all, it is necessary to highlight the genes of cytokines, which have a very

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high variety of polymorphic variants located in the regulatory zones of the gene [12]. Among the wide range of these genes, the IL10 gene, which is located on the long arm of chromosome 1q31-32 and consists of five exons and three introns, is of particular importance [1]. It is known that the gene possessing an ability to suppress cell-mediated immune responses and cytotoxic inflammatory responses [10] , and also by stimulating the activity of T-helpers 2 (Th2) and B-lymphocytes, it leads to a decrease in the severity of inflammatory reactions [1]. Furthermore, according to foreign researchers through gain I regulation of IL -10 leads to the suppression of the activity of the immune response, conditions are created favorable to the survival of HbF - infection, which thus accompanied by increased inflammation in the mucosa of stomach and duodenum [3] .

The role of various polymorphic variants of the IL- 10 gene has been established in the development of a particular pathology of the stomach and duodenum in many studies [2 , 9]. In particular, research H . H . Cheng , the C . The S . Chang , H . J . Wang , W . The C . Wang (2010) demonstrated the presence of an association of the C / T genotype of the IL- 10 (819) gene with an increased risk of gastritis among Taiwanese patients [2] . Then both , results of studies CF Zambon , D. Basso, F. Navaglia , C. Belluco , A. Falda , P. Fogar , et al. (2005) show the presence of association genotype T / T gene IL -10 (819) from Italian patients with the development of intestinal metaplasia and noncardiac gastric cancer, as well as its absence with the development of peptic ulcer disease [10 , 1 4].

The synergistic effect of polymorphic variants of the IL-10-592A/A genes on the development of gastric carcinoma and gastric ulcer was established by M. Kang et al . (2009) [3].

Along with this, there is data indicating an absence and roles IL -10 in the development of inflammatory processes in the mucosa of stomach and duodenum [8]. In particular, the absence of statistically significant differences between the

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carriage of the IL- 10 gene (592) and the development of atrophic gastritis and non-cardiac bowel cancer are given in the publications of foreign researchers [1 3] . Similar data on the absence of the role of gene pro-inflammatory cytokine of IL -10 in increased or decreased risk of gastritis and peptic ulcer disease are set as in the studies of Iranian Researchers, M . Rezaeishahmirzadi et al . (2018). At the same time, the authors conclude that the role of the IL- 10 gene in inflammatory diseases has not yet been fully studied, and therefore these results cannot be considered conclusive and require additional studies [9] .

Thus, the presence of multidirectional results of studies to assess the role of IL 10 in the development of pathological processes in the stomach and duodenum undoubtedly require additional research in this area, because Identification of genes involved in the mechanisms of formation and development of GU and DU will allow not only to identify genetic risk factors for the development and severe course of the disease, but also to carry out early diagnosis, differentiated correction in treatment, as well as its prevention in the presence of a predisposition to this disease.

Purpose of the study. Evaluation of the significance of the gene regulator of inflammation IL10 (rs3024491) in predisposition to the development of gastric ulcer and duodenal ulcer**.**

Material and methods

The study included 100 adults (main group, median age - 4 8,8 ± 3.8 years) unrelated Uzbek patients diagnosed as gastric ulcer and duodenal according to current classification criteria (2010), patients took treatment in clinics Tashkent medical Academy period from 2019 to 2020 years. The main group depending on nosology's divided into two subgroups: Ia - subgroup - DU patients with (n = 69) and Ib - subgroup - GU patients (n = 51) . The control group consisted of conditionally healthy Uzbek donors (n=85) without inflammatory processes in the history is consistent with e sex and age group of patients surveyed. Informed

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consent was obtained from all patients, as well as from individuals of the control group.

DNA was isolated from venous blood leukocytes in accordance with the standard protocol for DNA isolation [6]. The detection of the rs3024491 polymorphism of the IL10 gene was carried out by SNP-PCR on a programmable thermal cycler from Applied Biosystems 2720 (USA), using test systems from Litech (Russia), according to the manufacturer's instructions. The specificity and the number of amplified fragments were checked by agarose gel electrophoresis. Statistical analysis of the results was carried out using the statistical software package "OpenEpi 2009, Version 9.3".

Results and discussion

The frequency distribution of the rs3024491 genotypes of the IL10 gene and their correspondence to the Hardy- Weinberg population equilibrium (RHB) was carried out separately in the study group and the control group .

It was shown that the distribution of the frequencies of the genotypes of s observed in the studied groups corresponded to the expected for RHB, as evidenced by the value of $p > 0.05$. The results obtained indicate the homogeneity of the studied sample. The test results correlate well with each other, which, taking into account the sample size, allows us to speak about the actual absence of deviations from RHB.

The study of the frequency distribution of alleles and genotypes of the polymorphic variant rs3024491 of the IL10 gene in the control group made it possible to register the proportion of the occurrence of the G allele in 71.2%, and the A allele in 28.8% of cases. The proportion of carriage of a favorable homozygous G / G genotype was recorded in 52.9% (n = 45), a heterozygous G / A genotype in 36.5% (n = 31), and a mutant homozygous A / A genotype in 10.6% (n = 9) of the examined relatively healthy persons (see Table 1).

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Table 1

Frequency of distribution of alleles and genotypes of polymorphism rs3024491 gene IL10 (G-1082A) in the control group and the main group of patients with PUD and DU

Group	n	Allele frequency				Genotype distribution frequency					
		G		AND		G / G		G / A		A / A	
		n	%	N	%	n	%	n	%	N	%
The main group of patients with duodenal ulcer	one hundred	147	73,5	53	26.5	57	57	33	33	ten	ten
Ia - subgroup of patients with duodenal ulcer	49	69	70.4	29	29.6	26	53.1	17	34,7	6	12.2
Ib - a subgroup of patients with GU	51	78	76.5	24	23.5	31	60.8	16	31.4	four	7.8
Control group	85	121	71.2	49	28.8	45	52.9	31	36.5	9	10.6

Analysis of the proportion of the frequency of alleles and genotypes of the rs3024491 polymorphism of the IL10 gene in the main group of patients (n = 100) showed that the proportion of allele G was found in 73.5% (n = 147), and allele A - in 26.5% (n = 53). In the main group of patients, the proportion of the frequency of the homozygous genotype G / G was 57% (n = 57), the heterozygous genotype G / A - 33% (n = 33) and the mutant genotype A / A - 10% (n = 10) of the cases.

Analysis of the frequencies of alleles and genotypes of the rs3024491 polymorphism of the IL10 gene, depending on the nosology, made it possible to establish the following data:

in I and - a subgroup of patients share allele G was somewhat lower values

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(70.4%) and allele contrary exceeded (29.6%), those patients in the main group. A similar picture was observed in relation to the shares of genotypes G / G (53.1%), G / A (34.7%), and A / A (12.2%).

in Ib - subgroup of patients allele G in comparison with the I and subgroup encountered more frequently (76.5%) and allele A less frequent (23.5%). With regard to the frequencies of genotypes, a similar trend was observed, as well as with respect to the frequencies of occurrence of alleles: genotype G / G (60.8%), genotype G / A (31.4%), and genotype A / A (7.8%).

Comparative assessment of differences in the proportion of alleles and genotypes of the rs3024491 polymorphism of the IL10 gene made it possible to establish the absence of statistically significant differences between the control group and the main group of patients with ulcerative disease. Thus, the difference frequency of allele G in the study group of patients with ulcer as compared with the frequency in the control group was 1,12 (p > 0. 05 , O R = 1.12; 95% C I: 0.71-1.77), regarding the frequency of allele A it is less than unity (p > 0.05 ; O R = 0. 9 , 95% C I: 0.56- 1.41). As for the differences in genotype frequencies, then, similarly, no significant differences were found: G / G (p > 0.05 ; O R = 1. 2 , 95% C I: 0.66-2.11), G / A (p > 0.05 ; O R . = 0 9 95% C I: 1.57-0.47) and A / A (p > 0.05 ; O R = 0.94, 95% C I: 2.4 4 -0.36) (see Table 2).

T ABLE 2

Analysis of the difference in the frequency distribution of alleles and genotypes of the rs3024491 polymorphism of the IL10 gene (G-1082A) between the main group of patients with DU and the control group

Alleles and Genotypes	Main group n = 90		KG n = 95		Credibility
		%	n	%	
G	147	73 , 5	121	71, 2	p > 0.05; OR = 1.12; 95% CI : 0.71-

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A	53	26.5	49	28.8	1.77
G / G	57	57	45	52.9	p > 0.05; OR = 1 . 2 ; 95% CI : 0.66-2.11
G / A	33	33	31	36, 5	p > 0.05; OR = 0.9 ; 95% CI : 0.47-1.57
A / A	Ten	ten	9	10, 6	p > 0.05; OR = 0 . 94; 95% CI : 0.36-2.44

Evaluation of differences in the distribution of allele and genotype frequencies of rs3024491 polymorphism of the IL10 gene in comparison with the control group in the Ia - and Ib - subgroups of patients with ulcerative disease also showed no statistically significant differences in comparison with the proportion of allele and genotype frequencies in the control group. Thus, in the subgroup Ia of patients, the differences in the frequencies of the G and A alleles were 0.96 (p > 0.05; O R = 0.96; 95% C I: 1.6 5 -0.56) and 1.04 (p > 0.05; O R = 1.04; 95% C I: 0.60-1.79), the differences in the frequencies of the G / G genotypes were 1.0 (p > 0.05; O R = 1.0; 95% C I: 0.52-1.95), G / A - less than one (p > 0.05; O R = 0.93; 95% C I: 1.9 4 -0.44) and A / A - 1 2 (p > 0.05; OR = 1. 2 ; 95% CI: 0.39-3.53). Whereas in the Ib subgroup of patients, the differences in the frequency of the G and A alleles were 1.32 (p > 0.05; OR = 1.32; 95% CI: 0.75-2.31) and less than one (p > 0.05; OR = 0.76; 95% CI: 1.34 - 0.43). Along with this, the differences in the frequencies of the genotype G / G made 1. 4 (p > 0.05 ; OR = 1. 4 , 95% CI: 0.68-2.79), G / A (p > 0.05 ; OR = 0.8; 95% CI : 1.67-0.38) and A / A (p > 0.05; OR = 0.72; 95% CI: 2.45-0.21).

In addition, we assessed the differences in the distribution of the proportion of allele and genotype frequencies between Ia and Ib subgroups of patients. The established differences were also characterized by statistical insignificance in the

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distribution of alleles G (p > 0.05; OR = 0.73; 95% CI: 1.3 7 -0.39) and A (p > 0.05; OR = 1.37; 95% CI: 0.73-2.56) , as well as genotype G / G (p > 0.05; OR = 0.73; CI 95%: 1.61-0.33) , G / A (p > 0.05; OR = 1. 2 ; 95% CI: 0.5 1 - 2.6 7) and A / A (p > 0.05 ; OR = 1.64; 95% CI: 0.44-6.1 5) .

Thus, the study of the features of the frequency distribution of allelic and genotypic variants of the rs3024491 polymorphism of the IL10 gene showed the absence of their association with the development of GU and DU.

These facts can be explained by the fact, perhaps by the peculiarities of the ethnicity of the patients, and also, in addition, it is necessary to take into account the fact that the factors participating in complex systemic processes work in interaction, providing the initiation, potentiation or inhibition of the function of individual systems, as well as functional compensation of one link by another, while directing the biological process along an alternative physiological path. In this regard , a change in one gene encoding a particular process may not have an effect on the entire system as a whole, however , a change in two or more genes can radically change the systemic process and cause the development of pathologies and . Therefore, when studying the association of genetic polymorphisms with the development of a disease, it is advisable to assess the influence of not one, but several genes.

Conclusion

It is known that genes regulating the immune response play a significant role in the pathogenesis of inflammation and the formation of peptic ulcer disease , and therefore , an active study of the participation of key cytokine genes in the mechanisms of disease development is being carried out [1] . To date, sufficiently reliable data have been accumulated on the involvement of various cytokine genes, the products of which are directly involved in the regulation of the immune response in inflammatory processes of the gastrointestinal tract [5] . However, among these works, studies devoted to the genetic mechanisms of the formation of gastric ulcer and duodenal ulcer

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(DU) are very controversial [1 2] . In addition, despite the undeniable presence of common patterns of immune responses during inflammatory and erosive process, it is still not revealed genes common determinants of predisposition to the development of inflammation and GU and DU duodenum. In this regard, in this study , we also assessed the degree of participation of the rs3024491 polymorphism of the IL-10 gene in the development of GU and DU. Analysis of the results revealed that both main group and the subgroups of patients with GU and DU incidence allelic and genotypic variants polymorphism rs3024491 gene IL10 is characterized by the absence of significant statistical differences in comparison with those in the control group, indicating the absence and their association with development of GU and DU.

Analyzing to date the results of the studies carried out on the study of the molecular genetic mechanisms of the development of GU and DU, given their contradictory nature, it is obvious that the genetic mechanism of the development of the disease is complex, in which the role of any one gene is not great, and where most likely they play a significant role result reacting I few genes [7].

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