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RESULTS OF FREQUENCY ANALYSIS OF DEFB1 GENE -44C/G rs2412971 POLYMORPHISM IN DIFFERENT FORMS OF CHRONIC TONSILLITIS

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ABSTRACT

In the oral cavity, the tonsils are secondary lymphoid organs, representing tissues of local immunity, capable of providing a rapid and nonspecific response to pathogens, as well as triggering the action of the acquired immune system.

Despite their important role in fighting germs in the mouth, the tonsils can suffer from infections: due to their anatomical position, the tonsils are in constant contact with oral debris, foreign materials and pathogens, leading to chronic inflammation and enlargement of the tonsils. recurrent tonsillitis.

Recurrent tonsillitis has a multifactorial etiology, dependent on host and environmental factors: genetic control of the innate immune system represents a possible candidate to explain, at least in part, susceptibility to the disease.

Key words: chronic tonsillitis, hereditary factor, genetic factor, infectious-allergic diseases, phagocytosis, gene, polymorphism.

INTRODUCTION

Among all oral innate immune genes, genes encoding antimicrobial peptides are of particular interest; possible dysregulation of the production of these antimicrobial peptides may increase susceptibility to the development of oral pathologies [1,5,8].

Defensins have already been described as being involved in the maintenance of general oral health [9,10], having antibacterial, antifungal and antiviral activities, as well as immunomodulators and chemoattractant properties for immune cells [2,5]. In particular, beta-defensins, cysteine-rich antimicrobial peptides, can be considered important players in the defense against microbes in the oral environment.

The purpose of this publication is to study the frequency of occurrence analysis of DEFB1 gene -44C/G rs2412971 polymorphism in different forms of chronic tonsillitis.

Materials and methods: molecular-genetic methods were carried out in the Department of Molecular Medicine and Cell Technologies of GenoTechnology (Director Ph.D. Khujakhmedov J.D.).

This part of the research consisted of several stages:

1. Taking blood
2. Isolation of DNA from peripheral blood lymphocytes
3. Conduct PCR
4. Electrophoresis and visualization of results.

All patients were divided into 3 groups. The first group consisted of 64 patients with the diagnosis of chronic tonsillitis, simple form, the second group consisted of 55 patients with the diagnosis of chronic tonsillitis, toxic-allergic form 1 degree, and the third group consisted of 35 patients with the diagnosis of chronic tonsillitis, toxic-allergic form of the second degree.

Table 1 presents the prevalence values of alleles and genotypes of the -44C/G rs2412971 polymorphism of the DEFB1 gene.

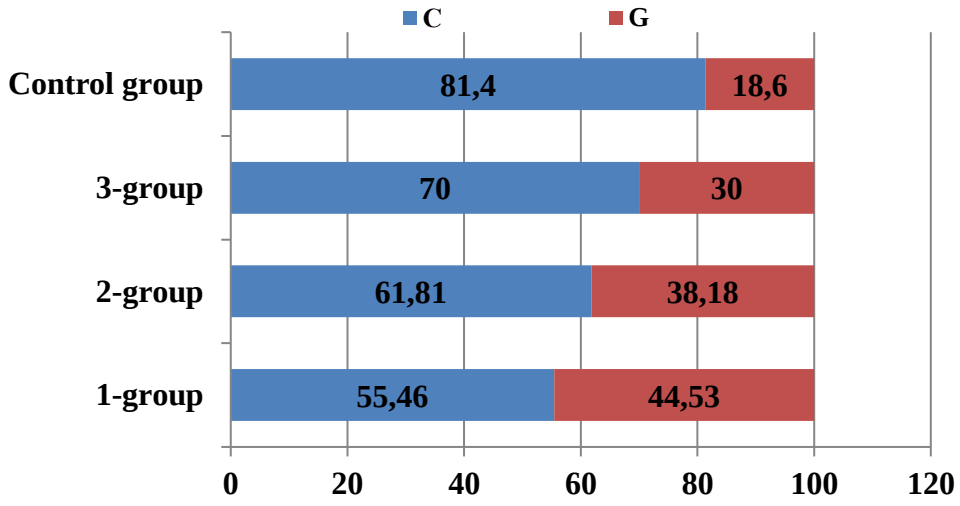
Table 1

Distribution frequency of alleles and genotypes of the DEFB1 gene -44C/G rs2412971 polymorphism.

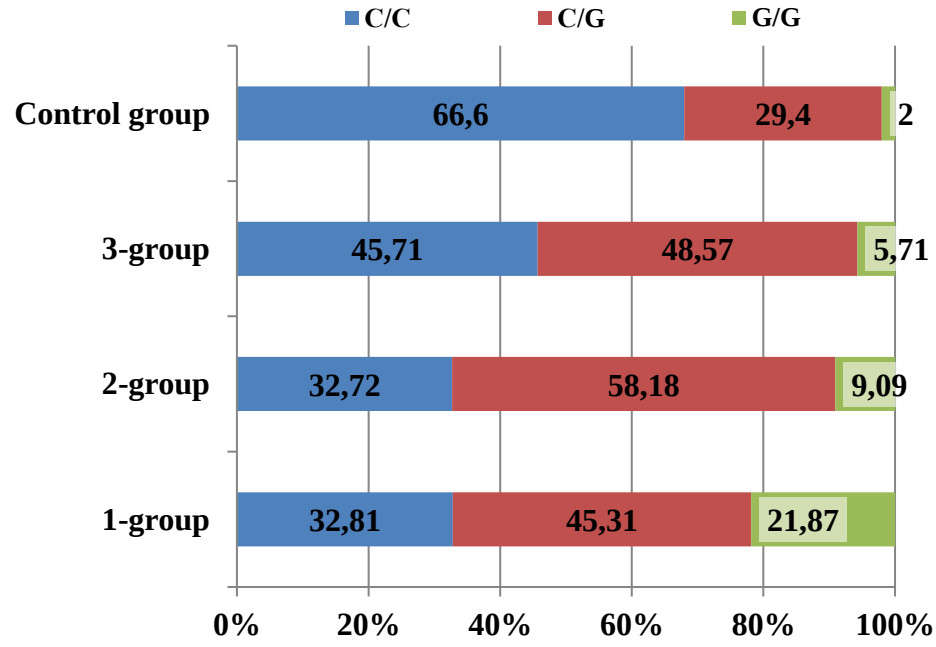
№	Group	Allele frequency				The distribution frequency of genotypes					
		C		G		C/C		C/G		G/G	
		n	%	n	%	n	%	n	%	n	%
1	1 group n=64	71	55.46	57	44.53	21	32.81	29	45.31	14	21.87
2	2 group n=55	68	61.81	42	38.18	18	32.72	32	58.18	5	9.09
3	3 group n=35	49	70	21	30	16	45.71	17	48.57	2	5.71
4	Control group n=51	83	81,4	19	18,6	**34**	66,6	**15**	29,4	**2**	2.0

Taking into account that allele G allele was dominant in all research groups, it should be remembered that the frequency of detection of G allele in group 1 was slightly higher compared to its values in group 2 and the control group. The detection frequency of the C allele, on the other hand, among the control group, was higher compared to its frequency in group 1 and group 2 patients.

The study of the distribution of genotypes showed that the C/C homozygous genotype was detected in the control group significantly, almost 2.8 times more often (66.6%), while the frequency of detection of the C/G heterozygous genotype was significant in 2 groups of patients (58.18%). Among all study groups, when studying the homozygous G/G genotype, it was possible to observe a 10.9-fold increase among patients in group 1 compared to the control group (Pic. 1,2).



Picture 1. Frequency of allele distribution of DEFB1 gene -44C/G rs2412971 polymorphism.



Picture 2. Frequency of prevalence of genotypes of DEFB1 gene -44C/G rs2412971 polymorphism.

On table 2. presents the results of the analysis of distribution of alleles and genotypes among patients in the control group and group 1.

Table 2

Differences in frequencies of alleles and genotypes of DEFB1 gene -44C/G rs2412971 polymorphism

Alleles and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+ 95%CI	OR	+95 %CI
	1 group		Control group							
	n	%	n	%						
C	71	55,5	83	81,4	1,2	0,01	0,7	0,45 - 1,04	0,3	0,16 - 0,52
G	57	44,5	19	18,6	1,2	0,01	1,5	0,65 - 3,31	3,5	1,94 - 6,34
C/C	21	32,8	34	66,7	1,0	0,01	0,5	0,24 - 1,02	0,2	0,11 - 0,52
C/G	29	45,3	15	29,4	3,0	0,10	1,5	0,83 - 2,87	2,0	0,92 - 4,31
G/G	14	21,9	2	3,9	7,6	0,01	5,6	3,29 - 9,45	6,9	1,75 - 26,88

The analysis showed that the detection frequency of the C allele had statistically significant differences in the control group (81.4%), but there was a significant trend of an increase in the detection of the G genotype among group 1 patients ($\chi 2$ =1.2; R=0.01; RR=1.5; OR=3.5; 95% CI: 0.65– 3.31).

The analysis of detection frequencies of the C/C genotype showed that this genotype among group 1 patients was statistically unreliable, i.e. more than 2.03 less frequently than in the group of conditionally healthy people ($\chi 2$=1.0; R=0.01; RR=0.5; OR =0.2; 95% CI: 0.24–1.02). The results of studying the distribution of C/G genotype among 1 group of patients compared to the control group revealed an insignificant and statistically unreliable prevalence - in this 1 group of patients, the detection frequency of this genotype in the control group of conditionally healthy people was 1.54 times higher ($\chi 2$=3.0; R=0.10; RR=2.0; 95% CI: 0.83-2.87). G/G genotype was markedly higher among patients in group 1, which was 5.61 times compared to the control group (Table 2.).

Table 3 shows that the results of the analysis of distribution of alleles and genotypes of DEFB1 gene -44C/G rs2412971 polymorphism in 2 groups of patients and among conditionally healthy people show the same indicators.

Table 3

Differences in frequency of alleles and genotypes of DEFB1 gene -44C/G rs2412971 polymorphism

Allele- and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+ 95%CI	OR	+95%CI
	2 group		Control group							
	n	%	n	%						
C	68	61,8	83	81,4	9,9	0,01	0,8	0,47 - 1,23	0,4	0,2 - 0,69
G	42	38,2	19	18,6	9,9	0,01	1,3	0,6 - 2,88	2,7	1,45 - 5,01
C/C	18	32,7	34	66,7	12,2	0,01	0,5	0,22 - 1,11	0,2	0,11 - 0,54
C/G	32	58,2	15	29,4	8,9	0,01	2,0	0,95 - 4,12	3,3	1,51 - 7,38
G/G	5	9,1	2	3,9	1,1	0,30	2,3	0,86 - 6,27	2,5	0,48 - 12,63

Analysis of the distribution of C and G alleles showed that in group 2, the C allele was slightly less than 1.31 times, more precisely, statistically unreliable in group 2 compared to the control group ($\chi 2$=9.9; R=0.01; RR=0.8; OR=0.4; 95% CI: 0.47 - 1.23), and the prevalence of G allele was more than 2.05 times more prevalent among 2 groups of patients ($\chi 2$=9.9; R=0.01; RR=1.3; OR=2.7; 95% CI: 0.6- 2.88).

Among conditionally healthy people, the C/C genotype was found to be reliable, i.e. 2.03 times higher than its detection frequency compared to 2 groups of patients ($\chi 2$ =12.2; R=0.01; RR=0.5; OR=0.2; 95% CI: 0.22-1.11).

In addition, it was found that the heterozygous C/G genotype was 1.97 times higher than the control group in 2 groups. A significant result was the prevalence of the G/G homozygous genotype among the 2 groups of patients compared to the control group, and a statistically significant prevalence was noted ($\chi 2$ =1.1; R=0.30; RR=2.3; OR=2.5; 95% CI: 0.86- 6.27).

Table 4 shows the results of the analysis comparing the prevalence of DEFB1 gene -44C/G rs2412971 polymorphic locus alleles and genotypes among 3 groups of patients to the control group.

The analysis of the prevalence of C alleles in 3 groups of patients did not reveal statistically significant differences in the frequency of their detection, in the control group it was slightly superior by 1.16 times, it was 81.4% compared to 70.0%. Thus, the G genotype did not have significant and statistically reliable differences in both study groups, only it increased very insignificantly among the 3 groups of patients (1.61 times higher was noted).

Table 4

Differences in the frequencies of DEFB1 gene -44C/G rs2412971 polymorphism alleles and genotypes

Allele- and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+ 95%CI	OR	+95 %CI
	3 group		Control group							
	n	%	n	%						
C	49	70,0	83	81,4	3,0	0,10	0,9	0,42 - 1,77	0,5	0,26 - 1,08
G	21	30,0	19	18,6	3,0	0,10	1,2	0,58 - 2,31	1,9	0,92 - 3,8
C/C	16	45,7	34	66,7	3,7	0,10	0,7	0,25 - 1,86	0,4	0,18 - 1,01
C/G	17	48,6	15	29,4	3,3	0,10	1,7	0,62 - 4,38	2,3	0,93 - 5,51
G/G	2	5,7	2	3,9	0,2	0,70	1,5	0,2 - 10,65	1,5	0,2 - 10,95

At the same time, it was noted that the G genotype had insignificant differences in the frequency of distribution, insignificant superiority among 3 groups of patients ($\chi2$=3.0; R=0.10; RR=1.2; OR=1.9; 95% CI: 0.58-2.31).

The frequency of the C/C genotype was statistically unreliable, less than 1.45 times, among the 3 groups of patients compared to the control group ($\chi2$=3.7; R=0.10; RR=0.7; OR=0.4; 95% CI: 0.25-1.86).

C/G genotype, on the other hand, was detected at a non-significant level, i.e. 1.65 times more often among the 3 groups of patients ($\chi2$ =3.3; R=0.10; RR=1.7; OR=2.3; 95% CI: 0.62-4.38).

Differences in the frequency of detection of G/G genotype in 3 and control groups were statistically unreliable, and the value of this indicator was 1.46 times higher in patients of 3 groups compared to the control group ($\chi2$=0.2; r=0.70; RR=1.5; OR=1.5; 95 % CI: 0.2–10.65).

Thus, the G negative allele of the -44C/G rs2412971 polymorphism of the DEFB1 gene is more common in group 1 patients than in healthy individuals and groups 2-3. A high frequency of this allele was observed with a homozygous G/G variant predominance (5.61 times). However, the difference between patients in group 1 and those in the control group was noted at the level of trend, and the trend was at the threshold level of statistical significance. These data allow us to conclude that the G/G genotype of the -44C/G rs2412971 polymorphism of the

DEFB1 gene predisposes to the development and clinical course of chronic tonsillitis. This polymorphism is located in the promoter part of the gene and is included in the functional polymorphism. In patients with chronic tonsillitis, the presence of the C allele is accompanied by a decrease in the expression of the DEFB1 gene in the presence of the C/C genotype. Inflammatory response gene patterning can alter the immune and inflammatory response toward an inappropriate hyperinflammatory response, leading to the onset and progression of a more severe form of chronic tonsillitis.

The absence of significant differences in the prevalence of DEFB1 gene -44C/G rs2412971 genotypes among conditionally healthy donors and 2-3 groups of patients and the presence of unfavorable polymorphism can be explained by the fact that it is not enough for the development of this disease by itself. In genetically predisposed individuals, chronic tonsillitis develops according to the scheme of interaction in the "genotype-phenotype" system (genetic-environmental). At the same time, the presence of unfavorable genotypic variants can affect the clinical course of the disease.

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