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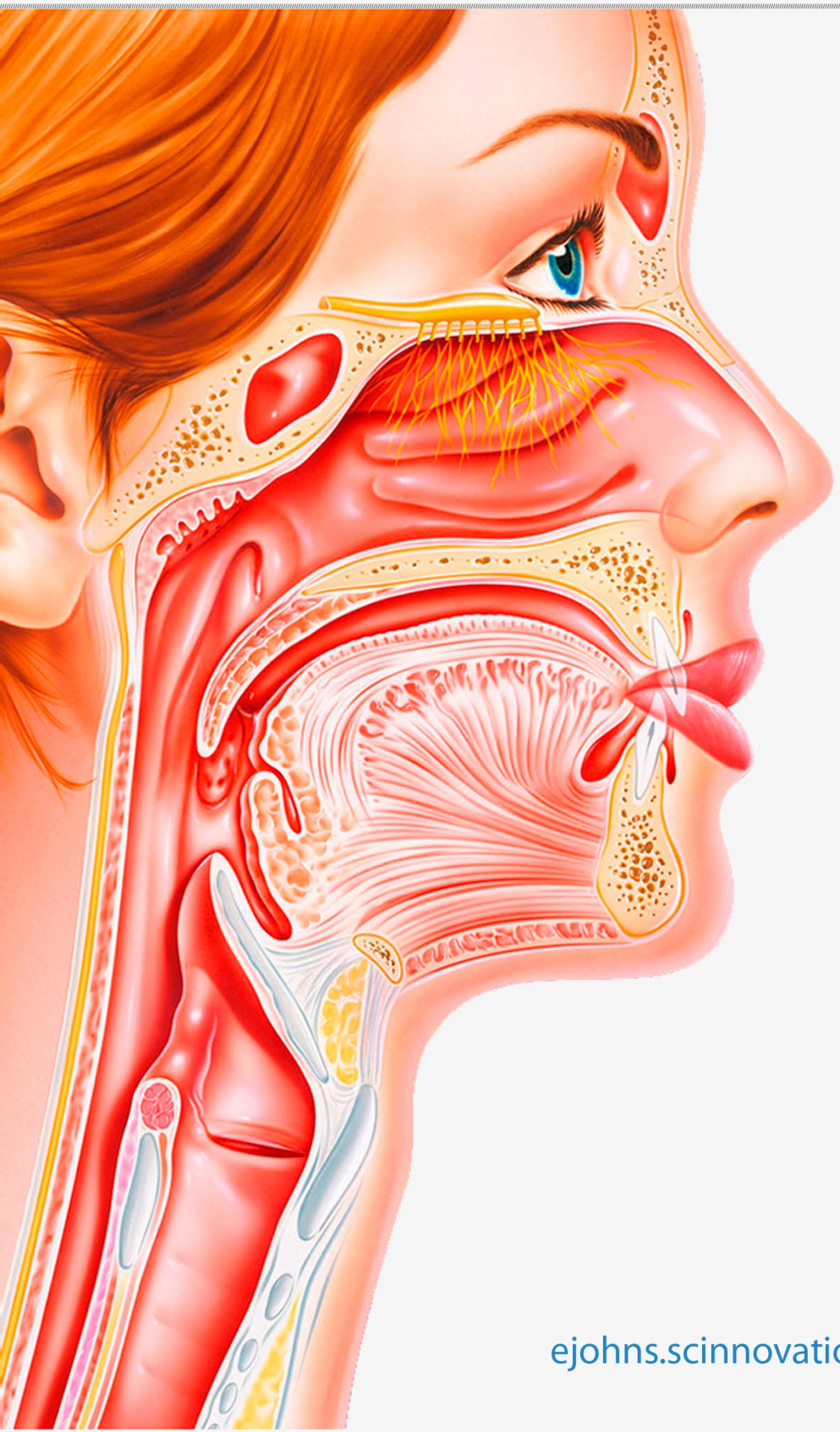

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RESULTS OF THE FREQUENCY OF OCCURRENCE OF ALLELES AND GENOTYPES OF THE RS2412971 745G>A HORMAD2 GENE POLYMORPHISM IN VARIOUS FORMS OF CHRONIC TONSILLITIS

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Abstract. The palatine tonsils are part of a collection of lymphoid tissues that are located at the entrance to the respiratory and digestive tracts. Anatomically, the structure of their crypts greatly increases the epithelial surface area available for contact with environmental agents, which, together with their strategic location, makes the tonsils the first part of the immune system to respond to antigens [1,2,3]. Chronic tonsillitis is a very common disease among adults and children, and is also part of hereditary diseases, or so-called multifactorial diseases. In this regard, to clarify the reasons for the development of this pathology, it is not unimportant to study the heredity of the development of chronic tonsillitis [4,5]. Some researchers believe that the cause of the development of chronic tonsillitis is a hereditary factor, while others pay more attention to the genetic factor in the development of this disease [6,7].

Keywords: chronic tonsillitis, hereditary factor, genetic factor.

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РЕЗУЛЬТАТЫ ЧАСТОТЫ ВСТРЕЧАЕМОСТИ АЛЛЕЛЕЙ И ГЕНОТИПОВ ПОЛИМОРФИЗМА ГЕНА RRS2412971 745G>A HORMAD2 ПРИ РАЗЛИЧНЫХ ФОРМАХ ХРОНИЧЕСКОГО ТОНЗИЛЛИТА

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Аннотация. Небные миндалины являются частью совокупности лимфоидных тканей, которые расположены у входа в дыхательный и пищеварительный тракты. Анатомически строение их крипт значительно увеличивает площадь поверхности эпителия, доступную для контакта с агентами окружающей среды, что, наряду с их стратегическим расположением, делает миндалины первым звеном иммунной системы, реагирующим на антигены [1,2,3].

Хронический тонзиллит является очень распространенным заболеванием среди взрослых и детей, а также является частью наследственных заболеваний, или так называемых многофакторных заболеваний. В связи с этим для выяснения причин развития данной патологии немаловажным является изучение наследственности развития хронического тонзиллита [4,5]. Некоторые исследователи считают, что причиной развития хронического тонзиллита является наследственный фактор, в то время как другие уделяют больше внимания генетическому фактору в развитии этого заболевания [6,7].

Ключевые слова: хронический тонзиллит, наследственный фактор, генетический фактор.

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INTRODUCTION

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 [8].

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 [9,10,11].

Recurrent tonsillitis has a multifactorial etiology, dependent on host and environmental factors

[8]: genetic control of the innate immune system represents a possible candidate to explain, at least in part, susceptibility to the disease.

THE PURPOSE

To study the frequency of occurrence of alleles and genotypes of the rs2412971 745G>A HORMAD2 gene polymorphism in various forms of chronic tonsillitis.

MATERIAL 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.

Studying the frequency of detection of alleles and genotypes of the 745G>A polymorphism in the HORMAD2 gene showed differences in their distribution between the main and control groups (Table 1.).

RESULTS AND DISCUSSION

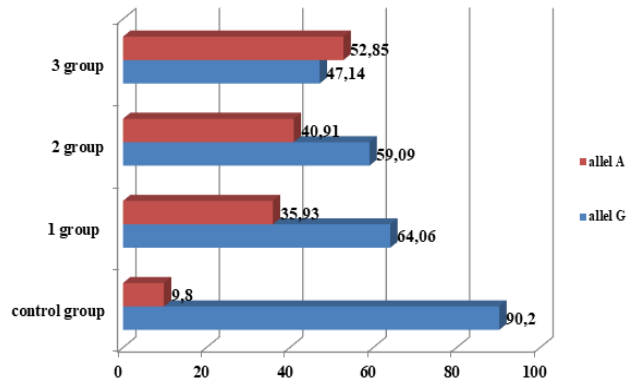
During the study, the detection frequency of G allele compared to A allele was 1.78 times higher in group 1, 1.44 times in group 2, and 9.2 times higher in the control group. In group 1, the G\G genotype was detected 3.4, 5.9, and 4.0 times more than the G\A and A\A genotypes, respectively, and in the control group, 7.6 and 2.1 times more, respectively (1, 2 - picture).

The results of the comparative analysis of the

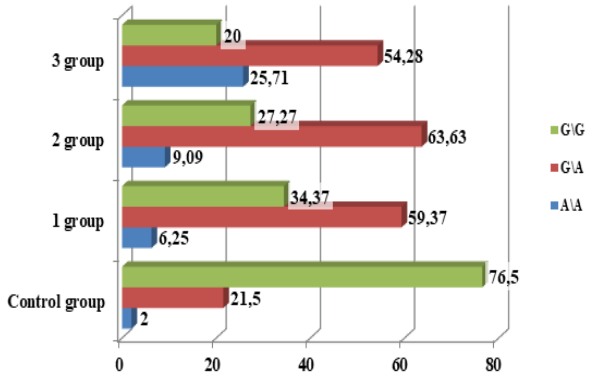
Table 1.

Frequency of alleles and genotypes of 745G>A polymorphism in HORMAD2 gene in patients

№	Group	Allele frequency				Distribution frequency of genotypes					
		G		A		G\G		G\A		A\A	
		n	%	n	%	n	%	n	%	n	%
1	1 group n=64	82	64.06	46	35.93	22	34.37	38	59.37	4	6.25
2	2 group n=55	65	59.09	45	40.91	15	27.27	35	63.63	5	9.09
3	3 group n=35	33	47.14	37	52.85	7	20	19	54.28	9	25.71
4	Control group n=51	92	90,2	10	9,8	39	76,5	11	21,5	1	2



Picture 1. Distribution frequency of alleles and genotypes of 745G>A polymorphism in HORMAD2 gene



Picture 2. Distribution frequency of alleles and genotypes of 745G>A polymorphism in HORMAD2 gene.

Table 2.
Differences in frequency of variants of alleles and genotypes of HORMAD2 gene polymorphism rs2412971 in group 1 patients and practically healthy individuals in the control group

Alleles and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+ 95%CI	OR	+95%CI
	1 group n=64		Control group n=51							
	n	%	n	%						
G	82	64,1	92	90,2	1,5	0,01	0,7	0,48 - 1,05	0,2	0,1 - 0,39
A	46	35,9	10	9,8	1,5	0,01	1,4	0,45 - 4,38	5,2	2,56 - 10,4
G/G	22	34,4	39	76,5	1,0	0,01	0,4	0,22 - 0,92	0,2	0,07 - 0,36
G/A	38	59,4	11	21,6	1,6	0,01	2,8	1,43 - 5,31	5,3	2,38 - 11,87
A/A	4	6,3	1	2,0	1,3	0,03	3,2	1,27 - 8,01	3,3	0,41 - 27,38

Table 3.
Differences in detection frequencies of HORMAD2 gene rs2412971 polymorphism alleles and genotypes in 2 groups of patients and control groups

Alleles and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+ 95%CI	OR	+95%CI
	2 group n=55		Control group n=51							
	n	%	n	%						
G	65	59,1	92	90,2	2,6	0,01	0,7	0,42 - 1,02	0,2	0,08 - 0,32
A	45	40,9	10	9,8	2,6	0,01	1,5	0,49 - 4,72	6,4	3,15 - 12,86
G/G	15	27,3	39	76,5	2,5	0,01	0,4	0,15 - 0,87	0,1	0,05 - 0,27
G/A	35	63,6	11	21,6	1,1	0,01	3,0	1,37 - 6,37	6,4	2,77 - 14,6
A/A	5	9,1	1	2,0	2,5	0,2	4,6	2,08 - 10,31	5,0	0,69 - 36,48

frequency of alleles and genotypes of the HORMAD2 gene polymorphism rs2412971 in patients are presented in Table 2.

As can be seen from the table, the frequency of detection of G genotype in group 1 patients compared to the control group was slightly lower, statistically unreliable ($\chi2=1.5$; r=0.01; RR=0.7; OR=0.2; 95% CI: 0.48-1.05). It was possible to note that the detection frequency of genotype A was 3.6 times more common among 1 group of patients. The detection frequency of the G/G genotype was 2.22 times higher in the majority of the control group, and its value was higher in the control group than in the 1 group of patients ($\chi2=1.0$; r=0.01; RR=0.4; OR=0.2; 95% CI: 0.22 -0.92). The frequency of G/A genotype in group 1 patients was about 2.75 times higher than in the control group and was 59.4% and 21.6%, respectively ($\chi2=1.6$? r=0.01; RR=2.8; OR=5.3; 95% CI: 1.43–5.31). The detection frequency of the A/A genotype was 6.3% among group 1 patients, which is a statistically reliable indicator and is 3.15 times higher than the population sample ($\chi2=1.3$; r=0.03; RR=3.2; OR=3.3; 95 % CI: 1.27–8.01).

Table 3 presents the results of a comparative analysis of the detection frequencies of HORMAD2 gene rs2412971 polymorphism alleles and genotypes in 2 groups of patients and the control group.

The frequency of occurrence of HORMAD2 gene polymorphism rs2412971 G allele was statistically unreliable and was found to be 1.52 times lower among healthy individuals ($\chi2=2.6$; r=0.01; RR=0.7; OR=0.2; 95% CI: 0.42-1.02) was recorded. The G/G genotype in the population sample was detected 2.8 times more often than in 2 groups of patients, which is a statistically unreliable difference ($\chi2=2.6$; r=0.01; RR=0.4; OR=0.1; 95% CI: 0.15-0.87). The frequency of determining the G/A genotype was

Table 4.
Differences in detection frequencies of HORMAD2 gene rs2412971 polymorphism alleles and genotypes in 3 groups of patients and the control group

Alleles and genotypes	Number of tested alleles and genotypes				Xi2	P	RR	+95% CI	OR	+95%CI
	3 group n=35		Control group n=51							
	n	%	n	%						
G	33	47,1	92	90,2	3,7	0,01	0,5	0,27 - 0,99	0,1	0,05–0,2
A	37	52,9	10	9,8	1,8	0,01	1,9	0,64 - 5,73	10,3	4,95 – 21,51
G/G	7	20,0	39	76,5	2,6	0,01	0,3	0,06 - 1,05	0,1	0,03–0,2
G/A	19	54,3	11	21,6	9,8	0,01	2,5	0,95 - 6,65	4,3	1,73 – 10,8
A/A	9	25,7	1	2,0	11,4	0,01	13,1	6,3 - 27,29	17,3	3,31 – 90,6

statistically reliable and was 2.9 times higher among the 2 groups of patients than among healthy controls ($\chi2=1.1$; r=0.01; RR=3.0; OR=6.4; 95% CI: 1.37-6.37). A comparative analysis of the occurrence of A/A genotype showed a significant trend of increased frequency of detection among 2 groups of patients compared to the population sample, its values were 9.1% and 2.0%, respectively. Here, the A/A genotype was 4.5 times more frequent among patients of 2 groups than among controls ($\chi2=2.5$; r=0.2; RR=4.6; OR=5.0; 95% CI: 0.69-36.48).

Table 4 shows the results of the analysis of frequencies of alleles and genotypes of the HORMAD2 gene polymorphism rs2412971 among 3 groups of patients and the control group.

Among 3 groups of patients, the G allele frequency was 1.9 times lower for the distribution of alleles of the HORMAD2 gene rs2412971 polymorphism, i.e. 47.1% ($\chi2<3.7$; r>0.01; RR=0.5; OR=0.1; 95% CI: 0.27-0.99), G allele was more common in 3 groups of patients and was 52.9% ($\chi2<1.8$; r>0.01; RR=1.9; OR=10.3; 95% CI: 0.64-5.73). The detection frequency of the G/G genotype is statistically unreliable, that is, its value was 20.0% in group 3 and 76.5% in the control group, that is, 3.8 times higher in the control group than in group 3 ($\chi2<2.6$; p >0.01; RR=0.1; 95% CI: 0.06-1.05). The frequency of G/A genotype was statistically unreliable, it was 54.3% among 3 groups of patients, i.e. 2.51 times higher than the control group ($\chi2<9.8$; r>0.01; RR=2.5; OR=0.82; 95 % CI: 3.29–2.62). It was found that the occurrence of A/A genotype in 3 groups of patients was reliably 12.85 times higher than the control group, i.e. 25.7% ($\chi2<11.4$; r>0.01; RR=13.1; OR=17.3; 95% CI: 6.3-27.29).

CONCLUSION

Thus, the unfavorable A allele of the HORMAD2 gene rs2412971 polymorphism is more common in 3 groups of patients compared to healthy people. A high frequency of this allele was noted in patients of groups 1, 2 and 3, with the predominance of the homozygous G/G variant (from 2.2 to 3.8 times). At the same time, the difference between patients of groups 1-2 and 3 and practically healthy individuals in the control group was noted at the level of tendency, and the tendency was at the threshold level of statistical significance. These data allow us to conclude that the A allele and G/A and A/A genotypes of the HORMAD2 gene rs2412971 polymorphism, associated with a decrease in HORMAD2 production, predispose to the development and clinical course of chronic tonsillitis. Since this polymorphism is located in the promoter region of the gene and belongs to functional polymorphisms, it can be argued that its presence affects the expression rate of the gene encoded by HORMAD2. Inflammatory response gene expression can change the immune and inflammatory response of the palatal cortex in the direction of an inadequate hyperinflammatory response, leading to the development of more severe chronic tonsillitis.

CONFLICT OF INTERESTS

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