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RESULTS OF THE FREQUENCY OF OCCURRENCE OF ALLELES AND GENOTYPES OF THE RS3124954 986CT FCN2 GENE POLYMORPHISM IN VARIOUS FORMS OF CHRONIC TONSILLITIS

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ABSTRACT

The problem of treating chronic tonsillitis (CT) remains relevant in modern medicine, which is determined by the widespread prevalence of this disease, as well as the likelihood of developing serious complications and chronic diseases of the cardiovascular system, kidneys and joints. The incidence of CT in children has reached 25% of the total incidence in the structure of ENT diseases. One of the key links in the pathogenesis of infectious and infectious-allergic diseases, which include chronic tonsillitis, is the interaction of microorganisms with leukocytes (phagocytosis). In this case, bacteria secrete factors that inhibit the activation of complement, the activity of lysozyme, interferon, which affects their ability to survive in the conditions of the macroorganism and resistance to phagocytosis.

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

INTRODUCTION

Chronic tonsillitis is one of the most common diseases encountered in everyday pediatric practice, which is the reason for continued study of this disease. In addition, among specialists there are different opinions about the methods of treating both acute and phonic tonsillitis. There are also difficulties in diagnosis [1,2,9,10]. Thus, recurrent tonsillitis occurring with elevated temperature should be classified as chronic. In such cases, upon examination, gross changes in the tonsils are detected: they are enlarged in size, and when pressed with a spatula, liquid purulent exudate appears [2,4,5,6,9]. The submandibular lymph nodes are also hypertrophied. Despite this, the diagnosis is often very “relative” and is rarely established with certainty.

In complicated cases and in cases of disability, surgical intervention is usually indicated. However, there are a number of patients who should or can avoid it.

These include, first of all, children with lymphatic diathesis. In addition, there are objective contraindications to the operation or the patient's subjective negative attitude towards it. In such cases, drug treatment is indicated, as well as in the preoperative and postoperative period [1,3,4,7,10].

Research objective: is to study the frequency of occurrence of alleles and genotypes of the rs3124954 986CT FCN2 gene polymorphism in various forms of chronic tonsillitis.

Material and methods of the study.

The geometric characteristics of the ethmoidal labyrinth were studied on CT images and their relationship with CRSwNP was examined. The study involved 142 children with various nasal cavity and paranasal sinus pathologies.

All children underwent a general clinical examination, including: general blood analysis, general urine analysis, anterior and posterior rhinoscopy, endoscopic rhinoscopy, and computed tomography. Based on the data from this examination, the patients were divided into three groups:

1. The group of conditionally healthy children included 30 children who were admitted to the ENT department with suspicion of nasal cavity and paranasal sinus diseases. Examination did not reveal any structural disorders of the ostiomeatal complex or any nasal disorders in them.

2. The group of patients with morpho-anatomical features of the ostiomeatal complex, conditionally called prone to developing nasal polyps (PDNP), included 32 children. These patients had the following ostiomeatal complex disorders: deviation of the uncinate process (13), deviation of the nasal septum in the cartilaginous part (13), concha bullosa (3), hypertrophy of the ethmoid bulla (4), crest or spur in the posterior parts of the nasal septum (12), hypertrophy of the posterior ends of the inferior nasal concha (12).

3. A group of patients with CRSwNP consisted of 80 children. This group included patients with recurrent CRSwNP (22 children) and polyposis-purulent form (58). During rhinoscopy, polypous overgrowths were observed in the middle or upper nasal passages. According to CT data, polyps filled the entire volume of the ethmoidal cells, the walls between the septa were thin, and there was thickening of the mucous membrane in the maxillary sinuses. The frontal and sphenoid sinuses were clear.

Endoscopic examination revealed deviation of the nasal septum to one side (31), signs of chronic sinusitis (21), vasomotor rhinitis (9), chronic hypertrophic rhinitis (19), as well as changes in the osteomeatal complex: deviation of the uncinate process - 30, concha bullosa - 28, hypertrophy of the ethmoidal bulla - 22,

deviation of the nasal septum in the anterior and posterior parts - 54, hypertrophy of the posterior ends of the inferior nasal turbinate - 33 children.

Children from the last two groups complained of difficulty breathing through the nose, mucous or mucopurulent nasal discharge, and hyposmia.

The areas of the ethmoidal cells were calculated on CT images for all patients, by cell groups and overall. The study of the entire set of images obtained from computer tomography allowed us to hypothesize a connection between the size of the ethmoidal cells and CRSwNP.

Molecular-genetic methods were carried out in the Department of Molecular Medicine and Cell Technologies of GenoTechnology.

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.

Research 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.

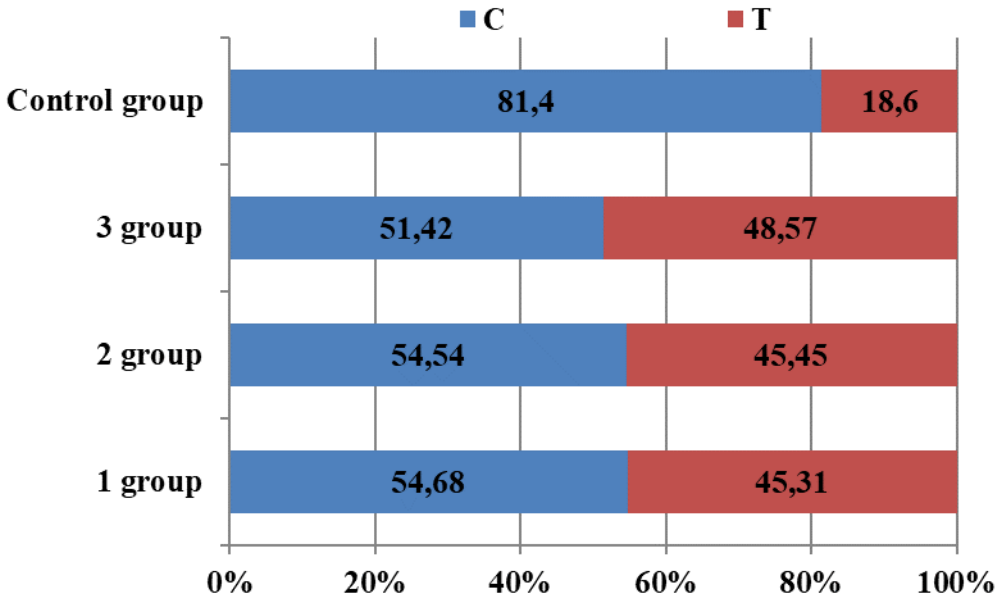
The distribution of alleles and genotypes of the rs3124954 polymorphism in the FCN2 gene among patients and conditionally healthy people was studied, the results of which are presented in Table 1

Table 1.

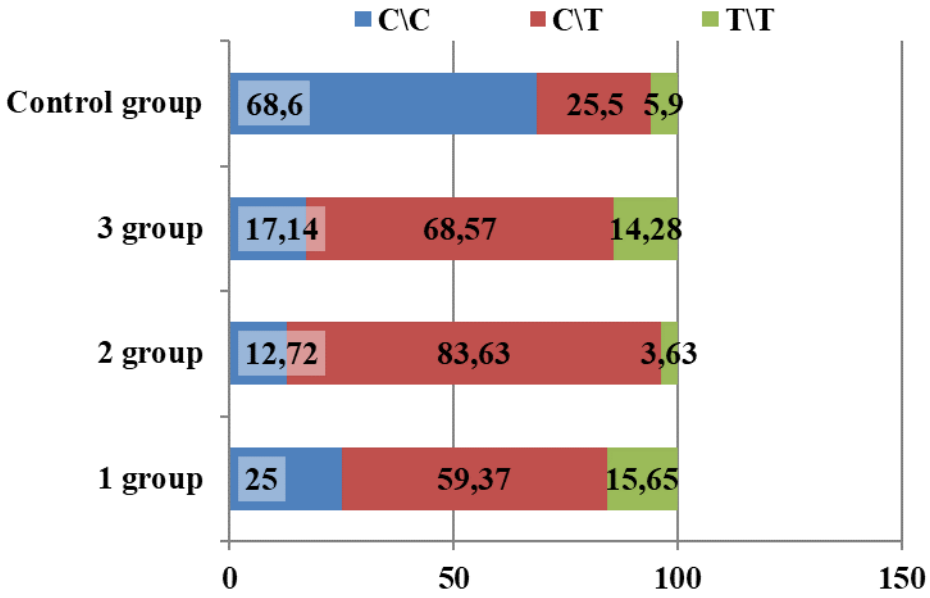
Prevalence frequency of alleles and genotypes of the rs3124954 -986CT polymorphism in the FCN2 gene among patients and in the control group

№	Group	Frequency allele				Genotype distribution frequency					
		C		T		C\C		C\T		T\T	
		n	%	n	%	n	%	n	%	n	%
1	1 group n=64	70	54.68	58	45.31	16	25.0	38	59.37	10	15.65
2	2 group n=55	60	54.54	50	45.45	7	12.72	46	83.63	2	3.63
3	3 group n=35	36	51.42	34	48.57	6	17.14	24	68.57	5	14.28
4	Control group n=51	83	81,4	19	18,6	**35**	68,6	**13**	25.5	**3**	5,9

On table 1 shows that in groups 1, 2 and 3, the prevalence of C allele is higher than T allele, C allele is 54.68%, 54.54% and 51.42%, respectively, T allele is 45.31 % was 45.45% and 48.57%. In general, the manifestation of differences was insignificant among patients of groups 1, 2 and 3 (Pic. 1, 2).



Picture 1. Prevalence of alleles of the rs3124954 -986CT polymorphism in the FCN2 gene.



Picture 2. Frequency of genotypes of rs3124954 -986CT polymorphism in FCN2 gene.

Also, prevalence of C/C, C/T and T/T genotypes of rs3124954 -986CT polymorphism in FCN2 gene was investigated. In group 2, the homozygous C/C genotype was detected at the highest frequency, its detection rate was 68.6%. Slightly lower values of this indicator were obtained in the study of the frequency of heterozygous C/T genotype, which was 83.63% in 2 groups of patients

(Table 1). Among 2 groups of patients, low indicators (3.63%) were found in the study of T/T genotype, this indicator was high (15.65%) in 1 group of patients.

Studying the distribution of genotypes in the population group revealed differences between the meeting values of genotypes with insignificant differences for group 2. Also, the highest detection rate - 68.6% was found in the study of the homozygous C/C genotype among conditionally healthy people, as well as in the control group. 1 group of patients was characterized by a small indicator equal to 59.37% for C/T heterozygous genotype (Table 2).

Table 2.

Differences in frequency of occurrence of rs3124954 -986CT alleles and genotypes polymorphism in FCN2 gene

Allele- and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+95%CI	OR	+95%CI
	1 group		Control group							
	n	%	n	%						
C	70	54,7	83	81,4	1,2	0,01	0,7	0,44 - 1,02	0,3	0,15 - 0,5
T	58	45,3	19	18,6	1,2	0,01	1,5	0,66 - 3,37	3,6	2 - 6,54
C/C	16	25,0	35	68,6	1,9	0,01	0,4	0,16 - 0,85	0,2	0,07 - 0,34
C/T	38	59,4	13	25,5	1,2	0,01	2,3	1,2 - 4,51	4,3	1,95 - 9,35
T/T	10	15,6	3	5,9	2,7	0,20	2,7	1,34 - 5,27	3,0	0,81 - 10,86

The results of the comparative analysis of the meeting of alleles and genotypes are presented in Table 2.

Comparison of the frequency of alleles showed that the C-allele was statistically slightly more frequent in the control group than in group 1 ($\chi 2$=1.2; R=0.01; RR=0.7; OR=0.3; 95% CI: 0.44-1.02). Comparison of allelic distribution frequencies showed that the T-allele was statistically significantly more frequent among group 1 patients than in the control group (45.3% among group 1 patients and 18.6% in the control group). The T/T genotype was detected in a statistically unreliable lower number of patients in group 1 than in the control group (25% among patients in group 1 and 68.6% in the control group). Analyzes of the frequency of the heterozygous C/T genotype showed a 2.3 times higher frequency of its occurrence among patients in group 1 ($\chi 2$=1.2; R=0.01; RR=2.3; OR=4.3; 95% CI: 1.2-4.51). In the study of the prevalence of T/T homozygous genotype, it

was observed 2.6 times higher among patients in group 1 than in the control group (χ2=2.7; R=0.20; RR=2.7; OR=3.0; 95% CI: 1.34-5.27).

The results of the analysis of alleles and genotypes of rs3124954 -986CT polymorphism in the FCN2 gene in group 2 patients and the control group are presented in Table 3.

Table 3.

Differences in frequency of alleles and genotypes of rs3124954 -986CT polymorphism in FCN2 gene

Allele- and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+95%CI	OR	+95%CI
	2 group		Control group							
	n	%	n	%						
C	60	54,5	83	81,4	7,3	0,01	0,7	0,42 - 1,08	0,3	0,15 - 0,5
T	50	45,5	19	18,6	7,3	0,01	1,5	0,67 - 3,31	3,6	1,98 - 6,69
C/C	7	12,7	35	68,6	4,6	0,01	0,2	0,05 - 0,72	0,1	0,03 - 0,16
C/T	46	83,6	13	25,5	6,3	0,01	3,3	1,01 - 10,69	14,9	6,2 - 36,03
T/T	2	3,6	3	5,9	0,3	0,60	0,6	0,07 - 5,23	0,6	0,1 - 3,71

During the study, the frequency of the C allele in patients in group 2 was 54.5%, which was found to be lower than in the control group, which was 81.4% (table 3.), the T allele was statistically dominant in group 2 at 45.5%. Homozygous S/S genotype (χ2=4.6; R=0.01; RR=0.2; OR=0.1; 95% CI: 0.05- 0.72) and heterozygous C/T genotype 3.27-fold advantage among 2 groups of patients compared to conditionally healthy people had a tendency. The heterozygous T/T genotype was 1.63 higher in the control group than in the 2 groups of patients and was 5.9% (χ2=0.3; R=0.60; RR=0.6; OR=0.6; 95% CI: 0.07-5.23).

Table 4.

Differences in frequency of alleles and genotypes of the rs3124954 -986CT polymorphism in the FCN2 gene

Allele- and genotypes	Number of tested alleles and genotypes				Xi2	p	RR	+95%CI	OR	+95%CI
	3 group		Control group							
	n	%	n	%						
C	36	51,4	83	81,4	17,5	0,01	0,6	0,33 - 1,23	0,2	0,12 - 0,47

T	34	48,6	19	18,6	17,5	0,01	1,6	0,75 - 3,33	4,1	2,12 - 8,02
C/C	6	17,1	35	68,6	22,1	0,01	0,2	0,06 - 1,13	0,1	0,04 - 0,25
C/T	24	68,6	13	25,5	15,7	0,01	2,7	0,88 - 8,25	6,4	2,55 - 15,94
T/T	5	14,3	3	5,9	1,7	0,20	2,4	0,74 - 7,96	2,7	0,62 - 11,47

As can be seen from Table 4., T allele in 3 groups was 2.61 times higher than the control group, and C allele was 1.58 times higher in the control group than 3 groups. The homozygous C/C genotype also predominated in the control group (68.6%) in accordance with the above. The rates of heterozygous C/T and homozygous T/T genotypes prevailed among the 3 groups of patients compared to the control group (2.69 and 2.43 times).

Summarizing the obtained results, we can conclude that there are almost no significant differences in the frequency of detection of allelic and genotypic variants of the rs3124954 -986CT polymorphic locus in the FCN2 gene in groups 1, 3 and the control group. There is no significant contribution of this locus in the formation and development of any form of chronic tonsillitis. However, in 2 groups of patients, compared to the control group, there is a significant tendency to decrease the frequency of the T/T genotype.

The detection of this genotype at a non-significant level in patients of group 2 compared to patients of groups 1, 2 and 3 confirms the insignificant protective role of the genotypic variant of the rs3124954 986CT polymorphism in the FCN2 gene in relation to the development of chronic tonsillitis in patients (5.15%, 8.0% vs., $\chi 2=3.4$; RR=0.2; 95% CI: 0.03-2.58.

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