The Role of Genes Enzymes Xenobiotics in The Mechanisms of Formation of Heavy Severity Level of Allergic Diseases in Uzbekistan

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Keywords
Allergic skin diseases, Genes of enzymes of biotransformation of xenobiotics, Gene polymorphism, Clinic.

Allergic dermatosis occupies one of the leading places in structure of the general disease of a skin and hypodermic cellular tissue and makes 56.2 % among skin diseases [1,2,5,13]. On the basis of formation of allergic dermatosis lays interaction of various genetic factors with environmental factors [3,4,6-10,12]. One of the effective approaches to studying of mechanisms of allergic dermatosis development is connected with research of the genes, products which can be expressly or by implication involved in development of the given pathology [11,17-22].

The purpose of our researches is the studying of polymorphism of genes of enzymes of biotransformation of xenobiotics in patients with allergic skin diseases.

Material and Research Methods
Object and subject of research were the patients with allergic dermatosis (AID), samples of DNA of sick and healthy donors, gluten transfusion genes GSTM1 (1p13.3), GSTT1 (22q11.2) and Ile 105Val genes of the GSTP1 gene were the object and subject of the study. The study included 88 patients with AID age ranging from 5 to 67 years. Of these, 41 are women, 50 are men. The diagnosis in all patients is confirmed by the results of the clinical examination and laboratory researches.

All patients were surveyed, observed and passed treatment in branch of dermatology Medical Centre of Dermatovenerology and carried out molecular-genetic inspection of biomaterials on the basis of department of molecular medicine and cellular technologies of scientific research institute of haematology and blood transfusion of MinH of the Republic of Uzbekistan.

Figure 1: Electric phoregramme of genes detection GSTM1 and GSTT1 (459 items n. – gene GSTT1, 375 items n. – β - γλδωνγ, 213 о. v. – GSTM1).

Genet Mol Med, 2019
Figure 2: Detection of (A/G) gene polymorphism of glutathione S-transferase P1 (rs–1) mutation -1:
K - negative control; K+ positive control; 1,3,8,9 – wild type A/A; 2,4,5,6,7,10 – heterozygous genotype A/G.

At carrying out of genetic researches as comparison group population control was used, which has been presented by samples of DNA (n=72) conditionally healthy donors (without any signs of atopic diseases) from bank of DNA of the given department.

The statistical analysis of results is spent with use of a package of statistical programs «OpenEpi 2009, Version 2.3».

Results of Research
On age aspect patients with AID up to 14 years old have made – 13, 15-20-year olds – 12, 21-30 – 17, 31-40-year olds – 12, 41-50 – 10 and over 50 years old – 24 patients. Under the clinical form allergic dermatosis has been diagnosed accordingly among 88 patients, 49 patients with atopic dermatitis, 28 patients with nettle rush, 11 patients with allergic dermatitis. Taking into account index DIShS moderate severity level is diagnosed for 10 patients 17, 21-30 – 17, 31-40-year olds – 12, 41-50 – 10 and over 50 years old – 24 patients. Under the clinical form allergic dermatosis has been diagnosed accordingly among 88 patients, 49 patients with atopic dermatitis, 28 patients with nettle rush, 11 patients with allergic dermatitis. Taking into account index DIShS moderate severity level is diagnosed for 10 patients.

The obtained data testifies that deletional polymorphisms GSTM1 «0/0» in 38,8 % of cases and GSTT1 0/0 = 22,4 % of cases basically met in patients from heavy severity level (29,3 ± 0,5 point) diseases.

As follows from the figure, frequency of functional and zero genotypes GSTM1 and GSTT1 most often came to light in patients with heavy and moderate severity level. Thus, it is necessary to notice, that in patients with AID frequency not functional genotype GSTM1 «0/0» has appeared in 1,1 times above in comparison with the individuals, having functional GSTM1 «+» a genotype. (OR=1.1; 95% CI0). However, calculation of frequencies of distribution of zero genotypes of gene GSTM1 between patients of AID (the basic group) and the control has shown, statistically not significant distinctions (χ²=0.3; Π =0.1).

Table 1: Sequence of oligonucleotides primers used for carrying out PCR.

Table 2: Distribution frequency of alleles and polymorphism genotypes del/del genes GSTM1 and GSTT1 in groups of patients and control.

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Results of molecular-genetic researches of polymorphism of genes enzymes xenobiotics in patients with AID have revealed certain features of deletional polymorphism GSTM1 and GSTT1 (Table 2).

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So, frequency studying of alleles and genotypes of genes FBC taking into account severity level of allergic dermatosis drew the following features (Figure 3).
The frequency of the distribution of genotypes by RCS Ile 105 Val polymorphism of the GSTP1 gene in the main group of patients with ALD showed that the observed frequency of A / A genotypes was found in 47.7%, heterozygous A / G genotypes - 39.7% and homozygous - G / G - 13.6%, respectively, whereas the expected frequency of the genotypes of group A / A and heterozygous - were 44.9 and 44.2%, respectively, and G / G - in 10.8% of cases.

While in the control group of healthy individuals, the observed and expected frequency of A / G heterozygous genotypes was found in 19.4% and 19.7% of cases, and homozygous non-functional G / G genotypes in 1.4 and 1.2%, respectively.

The associations of "functionally unfavorable" A / G genotypes were identified (χ² = 6.9, P <0.05, OR = 2.6, 95% CI 1.264-5.382) and G / G (χ² = 8.0; P <0.05; OR = 11.2; 95% CI 1.421-88.43) with the development of allergic dermatoses.

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Molecular genetic studies showed that patients with allergic dermatosis have an increased frequency of occurrence of the association of "functionally unfavorable" genotypes A / G and G / G -39.7% and 13.6%, respectively. According to the odds ratio, the risk of developing AID in the main group in the presence of the G / A polymorphism (OR = 2.6; 95% CI 1.264-5.382) and G / G (OR = 11.2; 95% CI 1.421-88.43) is 1.9 and 12 times higher compared to the control healthy group. Such indicators in the studied groups were statistically significant (χ² = 6.9; P <0.05; χ² = 8.0; P <0.05).

Whereas, the G allele and hetero / homozygous genotypes of GSTM1 and GSTT1 between the investigated groups has not revealed statistically significant distinctions (p>0.05).

Table 3: Frequency distribution of combined genotypes of deletional polymorphisms genes GSTM1 and GSTT1 in the investigated groups.

<table>
<thead>
<tr>
<th>№</th>
<th>Groups</th>
<th>Allele frequency</th>
<th>Frequency distribution of genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A</td>
<td>G</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>1.</td>
<td>The basic group n=88</td>
<td>118</td>
<td>67.0</td>
</tr>
<tr>
<td>2</td>
<td>Contr. Group n=72</td>
<td>126</td>
<td>87.5</td>
</tr>
</tbody>
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Table 4: The distribution frequency of alleles and genotypes of Ile 105 Val polymorphism of the GSTP1 gene in groups of patients and controls.

Note: n- number of examined patients, n*- number of chromosomes studied.

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<th>Alleles and genotypes</th>
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<th>Allele frequency in the control group</th>
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<tr>
<td>Allel A</td>
<td>118</td>
<td>126</td>
<td>χ²=10.8;P&lt;0.05;OR=3.4;95%CI 1.6-7.4</td>
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<td>Allel G</td>
<td>58</td>
<td>18</td>
<td>χ²=16.5;P&lt;0.05;OR=0.2;95%CI 0.1186-0.4868</td>
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Table 5: Differences in the frequency of occurrence of alleles and genotypes of Ile 105 Val polymorphism of the GSTP1 gene in the main and control groups.

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**Conclusion**

Thus, results of research have shown, that in patients with allergic dermatosis the raised frequency of combined zero genotypes (GSTM10/0 + GSTT10/0) in comparison with population sample (6.8 % and 4.1 % accordingly) is marked. The obtained data testifies that in Uzbekistan individuals with combined zero genotypes of genes enzymes xenobiotics GSTM1 and GSTT1 have a tendency to risk of development of allergic dermatosis heavy severity level.

Whereas, the G allele and hetero / homozygous genotypes of Ile 105 Val polymorphism of the GSTP1 gene are significant markers of an increased risk of developing allergic skin diseases in Uzbekistan (P<0.05). Allele A and the functionally favorable A / A genotype are reliable protective markers for the development of pathology (χ² = 16.5; P<0.05; OR = 0.2; 95% CI 0.1186-0.4868).

**References**


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