The Study of the Role Polymorphism of the P2RY12 Gene rs 2046934 in the Pathogenesis of Disaggregation Thrombocytopathy

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ABSTRACT

Background: Thrombocytopathy (TP) is one of the dangerous pathologies related to the platelet’s function; widespread of them is disaggregation thrombocytopathy. Authors aimed to study the role of polymorphism of the P2RY12 and rs2046934 genes in the formation of individual accident of Uzbek nationality. Methods: The study was conducted (n=71) patients with disaggregation thrombocytopathy, which was observed in consultative outpatient clinic of Institute of Hematology and blood transfusion Ministry of health Uzbekistan. Results: the study showed that the unfavorable allele A association with risk of development of hemorrhagic syndrome in disaggregation thrombocytopathy. Conclusions: The frequency of A/A and G/A genotypes of the P2RY12 gene in our sample was somewhat comparable with the world data and is consistent with the assumption that they affect the development of hemorrhagic states in disaggregation thrombocytopathy.

Keywords: Disaggregation thrombocytopathy, gene, polymorphism, allele, hemorrhagic syndrome.

INTRODUCTION

Thrombocytopathy (TP) are one of the pathologies of the disorder in the function of platelets, widespread of them is disaggregation thrombocytopathy. Disaggregation thrombocytopathy (DTP) is divided into hereditary and acquired groups, characterized by stable, long-lasting functional, biochemical and morphological changes in platelets with normal or slightly reduced their number. The main clinical feature, which is the nasal, gingival, uterine and other bleeding, petechial bruising hemorrhages on the body.[1,2,4,9,14] The prevalence of hereditary forms of thrombocytopathies is approximately 3-5 per 100,000 population. Acquired platelet dysfunction observed much more often, and the incidence in recent years has increase, what is primarily due to the uncontrolled use of drugs, especially when trying to self-medication.[15,17] Literature data suggests that the cause of the symptoms of disaggregation thrombocytopathy diver: genetic predisposition; previous infections: viral and bacterial; vaccinations, etc.[1,7] Studies of genetic polymorphisms in various diseases are becoming increasingly important in modern medicine, due to the improvement of diagnostic methods, since it is violations at the molecular level are the trigger mechanism of the Genesis of multifactorial diseases. A number of foreign scientists have studied various genetic polymorphisms in road accidents that determine a particular role in the Genesis of the disease.[6,8,10,11,16] Data for the study of genetic changes in hereditary disaggregation thrombocytopathy in the available literature is rather scarce.[15,18] In particular there are a number of research in the world for the study of the involvement of polymorphism of the P2RY12 gene rs2046934 in the pathogenesis of thrombocytopathy.[4,12,13] In this regard, the aim of our work is to study the role of polymorphism of the P2RY12 gene rs2046934 the formation of the accident in individuals of Uzbek nationality.

MATERIALS & METHODS

For carrying out the detection of the genetic polymorphism of the P2RY12 gene rs2046934 in the study were included patients with DTP (n=71) Uzbek nationality (of these, hereditary accident (HTP) n=39 and acquired accident (ATP) n=32), which were observed in the consultative polyclinic of the Research Institute of Hematology and blood Transfusion of the Ministry of Health of the Republic of Uzbekistan. The control group consisted of healthy unrelated persons of Uzbek nationality.

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without pathology of haemostasis. Testing of polymorphism of the P2RY12 gene rs2046934 was carried out on programmable thermal cycler of "Applied Biosystems" company 2720 (USA), using test systems of the company "Liteh" (Russia), according to the manufacturer's instructions. Statistical analysis of the results was carried out using the package of statistical programs "Open Epi, Version 9.3".

Electrophoregram detection of polymorphism of the P2RY12 gene rs2046934 in the control group and in patients with road accidents. [Figure 1]

![Electrophoregram](image)

Figure 1: Specificity and number of amplified fragments were tested by electrophoresis in 4% agarose gel.

In this electrophoregram, G/A 2,6,8 and 17 heterozygous genotypes were noted; A/A 9 homozygous genotype; the remaining G/G 1,3,4,5,7,10-16 normal genotypes.

**RESULTS & DISCUSSION**

Analysis of the study of the distribution of allele frequencies and genotypes of polymorphism of the P2RY12 gene rs2046934 in the general group of patients revealed closer to a significant increase in the proportion of carriers of adverse allele A in comparison with the control group (22.5% vs. 16.7%, respectively, at \(\chi^2=0.88\); \(P=0.35\); RR=1.19; 95% CI 0.85-1.67; OR=1.57; 95% CI 0.61-4.03). In further study of this genotype, a subgroup of patients with HTP (23.1% vs 16.7% at \(\chi^2=0.88\); \(P=0.35\); RR=1.31; 95% CI 0.77-2.24; OR=1.67; 95% CI 0.57-4.86) and a subgroup of patients with ATP in relation to the control group (21.9% vs. 16.7% at \(\chi^2=0.43\); \(P=0.51\); RR=1.24; 95% CI 0.66-2.33; OR=1.46; 95% CI 0.47-4.53), respectively.

The carrier frequency of homozygous genotype A/A in the main and control groups was 5.6% and 0.0%, respectively. In this case, the risk of disaggregation thrombocytopathy (the main group of patients) with the carrier of this genotype is 1.8 at \(\chi^2=3.04\); \(P=0.08\); 95% CI 1.49-2.14, this indicates a trend towards association. In the subgroup of patients with HTP, the frequency of this allele was 2.48% \((\chi^2=4.18; P=0.041)\) and in the subgroup of patients with ATP 2.67% \((\chi^2=1.63; P=0.20)\), respectively. It is obvious that our results indicate an association between adverse heter/homozygous genotypes with the development of disaggregation thrombocytopathy.

The distribution frequencies of the rs2046934 polymorphism genotypes of the P2RY12 gene in both the study and control groups corresponded to the expected distribution according to the Hardy-Weinberg equilibrium (\(P>0.05\)).

<table>
<thead>
<tr>
<th>Nr</th>
<th>Group</th>
<th>n</th>
<th>Allele frequency</th>
<th>G %</th>
<th>A %</th>
<th>The frequency distribution of genotypes</th>
<th>G/G %</th>
<th>G/A %</th>
<th>A/A %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>General group</td>
<td>71</td>
<td>83.1</td>
<td>16.9</td>
<td>51</td>
<td>71.8</td>
<td>16</td>
<td>22.5</td>
<td>4</td>
</tr>
<tr>
<td>A</td>
<td>HTP</td>
<td>39</td>
<td>80.8</td>
<td>19.2</td>
<td>27</td>
<td>69.2</td>
<td>9</td>
<td>23.1</td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>ATP</td>
<td>32</td>
<td>85.9</td>
<td>14.1</td>
<td>24</td>
<td>75.0</td>
<td>7</td>
<td>21.9</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Control group</td>
<td>48</td>
<td>91.7</td>
<td>8.3</td>
<td>40</td>
<td>83.3</td>
<td>8</td>
<td>16.7</td>
<td>0</td>
</tr>
</tbody>
</table>

**CONCLUSION**

One of the promising approaches in determining the risk of development of disaggregation thrombocytopathy is the study of genetic markers determining the risk of development and course of the disease. With this in mind, it is undoubtedly of great scientific and practical interest to study the significance of polymorphisms of genes responsible for the functional activity of platelets, in particular of polymorphism of the P2RY12 gene rs2046934[12,13].

In conclusion, it should be noted that the frequency of A/A and G/A genotypes of the P2RY12 gene in our sample was somewhat comparable with the
world data and is consistent with the assumption that they affect the development of hemorrhagic states in disaggregation thrombocytopathy. Results inconsistent with data of other researchers do not contradict conclusions, and can have regional feature.

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