Development of ways to Correct Hyperlipidemia on the Basis of Studying the Polymorphism of Genes Responsible for Fat Metabolism in the Cardiovascular System

Relevance: Today, overweight and obesity remain one of the most important global health challenges in the world. Being overweight and obese causes not only the appearance of all people but also a number of diseases, including atherosclerosis and cardiovascular diseases, hyperton, ischemic and hemorrhagic stroke, as well as all other serious problems of internal organs. Development of methods for correcting hyperlipidemia based on polymorphism of genes responsible for fat metabolism in diseases of the cardiovascular system. Thus, in patients with cardiovascular diseases, hyperthyroidism was corrected for 7 genes out of three: cholesterol, HDL, and LDL levels were higher in the initial group and lower in the control group.

Key words: overweight, obesity, HDL and LDL, genes and genotypes, cardiovascular system.

Abstract: Today, overweight and obesity remain one of the most important global health problems in the world. Overweight and obesity are the cause not only of the appearance of all people but also of a number of diseases, including atherosclerosis and cardiovascular diseases, hyperton, ischemic and hemorrhagic stroke and all other internal organs. In addition, being overweight has a negative effect on the endocrine system and increases the risk factor for causing diabetes, however obesity can lead to male or female infertility. Non-adherence to diet and certain hereditary characteristics of the patient may contribute to the development of metabolic syndrome [1,11,15,19]. Today, overweight and obesity are among the top five risk factors for death. According to statistics, at least 3.4 million adults die each year due to overweight or obesity. In addition, 44% of overweight was found to be associated with diabetes, 23% with cardiovascular disease, and 7% with cancer [2,10,20].

The prevalence of obesity among children and adolescents is growing significantly in developed countries, with 23.8% among boys and 22.6% among girls. In Russia, about 25 percent of people of working age are obese and 30 percent are overweight. The prognosis for this condition is that by 2030, more than 2 billion people will be overweight and 1 billion will be obese [3,9,15,18].

Thus, according to the data in the literature, the nature of genes in overweight and obese people, their
dependence on hyperlipidemia, has not been fully studied, and a number of problems in the study of these genes are waiting to be resolved. One of the major global challenges is to study the link between genes that respond to overweight and obesity in hyperlipidemia. In the medical practice of Uzbekistan, ways to detect and correct the link between genes in hyperlipidemia in overweight and obesity have not been developed and are not used in practice. To overcome the above-mentioned shortcomings, it is necessary to continue scientific research, as the detection of genes in overweight and obesity is linked to hyperlipidemia and the prevention of diseases that cause it is of great importance in medical practice.

**Objective:** To develop ways to correct hyperlipidemia based on the polymorphism of genes responsible for fat metabolism in diseases of the cardiovascular system.

**Materials and methods:** Research was carried out on 54 overweight patients treated in different departments of the Bukhara Regional Multidisciplinary Medical Center in 2019-2020. Of the 54 patients surveyed, 30 were in the control group and 24 in the main group.

**Results:**

During the study, three genes - ADRB2 (rs1042713) A> G; ADRB3 (rs4994) Trp64Arg and PPARG2 (rs1801282) C34G were studied, as well as seven genotypes associated with them - A / A; A / G; Trp / Trp; Trp / Arg; C / G; C / C; The G / G meeting rate was also analyzed (Table 1).

**Table 1: The rate of occurrence of genes and genotypes depending on the age and sex of patients diagnosed with diseases of the cardiovascular system**

<table>
<thead>
<tr>
<th>Genes</th>
<th>Genotypes</th>
<th>Age</th>
<th>Sex</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADRB2 (rs1042713) A&gt;G</td>
<td>A/A</td>
<td>53.0</td>
<td>MG</td>
<td>27.5</td>
</tr>
<tr>
<td></td>
<td>A/G</td>
<td>52.3</td>
<td>MG</td>
<td>25.6</td>
</tr>
<tr>
<td>ADRB3 (rs4994) Trp64Arg</td>
<td>Trp/Trp</td>
<td>52.1</td>
<td>MG</td>
<td>26.5</td>
</tr>
<tr>
<td></td>
<td>Trp/Arg</td>
<td>59.0</td>
<td>MG</td>
<td>27.0</td>
</tr>
<tr>
<td>PPARG2 (rs1801282) C34G</td>
<td>C/G</td>
<td>53.3</td>
<td>MG</td>
<td>23.5</td>
</tr>
<tr>
<td></td>
<td>C/C</td>
<td>51.5</td>
<td>MG</td>
<td>28.7</td>
</tr>
<tr>
<td></td>
<td>G/G</td>
<td>57.0</td>
<td>MG</td>
<td>23.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>54.03</td>
<td>MG</td>
<td>26.0</td>
</tr>
</tbody>
</table>

Note: absolute in the picture, relative (%) in the denominator; MG - the main group; CG - control group.

The results showed that the rate of occurrence of genes and genotypes was observed in the main group between the ages of 51.5 and 59.0 (average age 54.03): in the control group between the ages of 23.0 and 28.7 (average age 26.0 years). While the age gradations on the cited genes were uniformly distributed, they were slightly different on the genotypes. While S / S (51.5 years), Trp / Trp (52.1 years), and A / G (52.3 years) genotypes were more common in relatively young patients, G / G (57.0 years) and Trp / Arg (59.0 years) genotypes were identified in slightly older patients. It was noted that there was a significant age difference between patients belonging to the main and control groups.

When analyzing the sex-related situation, the rate of occurrence of genes and genotypes in men belonging to the main (n = 32) and control (n = 8) groups was close to each other. ADRB2, (rs1042713) The occurrence rate of the A> G gene was the same in both groups, similar indicators were observed in the genes ADRB3 (rs4994) Trp64Arg and PPARG2 (rs1801282) C34G.
However, there was a slight difference between the groups in males in terms of genotype occurrence rate - Trp / Trp, C / G genotypes were more common in the main group than in the control group, while Trp / Arg, C / C and G / G genotypes were less common, respectively. It should be noted that among all 7 genotypes in the main group of men, the genotypes Trp / Trp (28 out of 32 cases, 87.5%), C / G (20 out of 32 cases, 62.5%) were more common than 50%. However, a higher incidence rate in the control group was observed only in the Trp / Trp genotype (8 out of 6 cases 75.0%).

In women, the results are slightly different from those in men. In the main group, genotypes of Trp / Trp (27 out of 27 cases, 100.0%), C / C (19 out of 27 cases, 70.4%), A / G (15 out of 27 cases, 55.6%) when the incidence rate was high, different results were obtained in women belonging to the control group - they had the highest genotypes of Trp / Trp (4 out of 7 cases, 57.1%). Trp / Trp in men in the main group; Trp / Arg; While C / G genotypes are more common, Trp / Trp, C / C, A / G genotypes are more common in women in the main group. In addition to the Trp / Trp genotype, the S / S and A / A genotypes should be noted in the women in this group, while the Trp / Trp genotype has crossed the 50% threshold in the control group.

The occurrence of genes and genotypes in terms of total number of patients repeated the above trend. It is noteworthy that the rate of occurrence of genotypes within genes varies. The / Trp genotype was significantly superior to the Trp / Arg genotype (94.6% to 10.2%, respectively), with a clear advantage in the PPARG2 (rs1801282) C34G gene over the S / G and G / G genotypes in the S / S genotype (52 respectively). 5% vs. 39.0% and 5.1%). Looking at the performance of the primary and control groups, we note that the Trp / Trp genotype is more common in both groups - 94.9% (n = 56) and 86.7% (n = 13), respectively.

Although a gender difference was observed in meeting percentages, no significant difference in meeting trend was detected (Figure 1).

Purple for the main group, Red for the control group

It can be seen that the Trp / Trp, C / C, A / G, and A / A genotypes differed in that both groups were more common than other genotypes, with the least common genotype being recognized as G / G.

The results showed that the gene and genotypes studied in the main group were observed to have different differences depending on the patients. No differences in patient height measurements were identified, indicating that they did not have correlation features across patients. It has been shown that these genes and genotypes are not related to the height of patients diagnosed with AIDS.

Similar indicators were obtained for TMI - Trp / Arg (average 31.0 units), G / G (average 30.0 units)
and A / A (average 31.0 units) genotypes in the main group; In the control group, all indicators were practically the same and no genes directly related to TMI were identified (Figure 2).

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**Figure 2.** Patients diagnosed with the cardiovascular system, the degree of occurrence of genes and genotypes in accordance with the indicators of body mass index, units

Thus, the rate of occurrence of genes and genotypes of patients diagnosed with NCDs was not related to their height, and no sharply differentiated numbers corresponding to genotypes were identified. However, specificities related to patient mass were observed. The results showed that the amount of cholesterol in the blood in the control group was within the norm in all cases (reference values from 3.1 μmol / l to 5.0 μmol / l). These values ranged from an average of 3.9 μmol / l to 4.5 μmol / l, which proved to be within the reference range.

<table>
<thead>
<tr>
<th>Genes</th>
<th>Genotypes</th>
<th>Cholesterol, m/mol/l</th>
<th>(3,1-5)</th>
<th>HDLP m/mol/l</th>
<th>(0,72-1,63)</th>
<th>LDLIP m/mol/l</th>
<th>(2,02-4,79)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MG</td>
<td></td>
<td>MG</td>
<td></td>
<td>MG</td>
<td></td>
</tr>
<tr>
<td>ADRB2 (rs1042713) A&gt;G</td>
<td>A/A</td>
<td>6.9±0,17*</td>
<td>4,3±0,16</td>
<td>2.93±0,3*</td>
<td>1,03±0,04</td>
<td>6.94±0,5*</td>
<td>2,54±0,19</td>
</tr>
<tr>
<td></td>
<td>A/G</td>
<td>7.1±0,13*</td>
<td>4,1±0,13</td>
<td>2.95±0,2*</td>
<td>1,08±0,05</td>
<td>6.97±0,3*</td>
<td>2,31±0,13</td>
</tr>
<tr>
<td>ADRB3 (rs4994) Trp64Arg</td>
<td>Trp/Trp</td>
<td>7.2±0,12*</td>
<td>4,2±0,12</td>
<td>2.94±0,2*</td>
<td>1,05±0,04</td>
<td>6.95±0,3*</td>
<td>2,41±0,14</td>
</tr>
<tr>
<td></td>
<td>Trp/Arg</td>
<td>7.4±0,3*</td>
<td>4,5±0,36</td>
<td>2.67±0,4*</td>
<td>1,04±0,04</td>
<td>7.04±0,2*</td>
<td>2,60±0,1</td>
</tr>
<tr>
<td>PPARG2 (rs1801282) C34G</td>
<td>C/G</td>
<td>7.05±0,11*</td>
<td>3,9±0,18</td>
<td>2.89±0,3*</td>
<td>1,08±0,04</td>
<td>6.91±0,6*</td>
<td>3,0±0,13</td>
</tr>
<tr>
<td></td>
<td>C/C</td>
<td>7.01±0,14*</td>
<td>4,3±0,16</td>
<td>2.97±0,2*</td>
<td>0,96±0,04</td>
<td>6.98±0,3*</td>
<td>2,29±0,14</td>
</tr>
<tr>
<td></td>
<td>G/G</td>
<td>6.9±0,12*</td>
<td>4,4±0,26</td>
<td>3.01±0,3*</td>
<td>1,43±0,14</td>
<td>7.03±0,2*</td>
<td>3,35±0,6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>7.05±0,12*</td>
<td>4,2±0,11</td>
<td>2.91±0,12*</td>
<td>1,10±0,03</td>
<td>6.97±0,2*</td>
<td>2,64±0,12</td>
</tr>
</tbody>
</table>

Note: AG - main group, NG - control group. * - a sign of reliability between the main and control groups.

The highest values of the control group corresponded to the Trp / Arg genotype (4.5 μmol / l) and the G / G genotype (4.4 μmol / l) of the PPARG2 (rs1801282) C34G gene, which belonged to the ADRB3 (rs4994) Trp64Arg gene. However, it should be noted that the results obtained were very close to each other in the control group, and no clearly different parameters were identified. In the main group, the difference was obvious (P <0.002), all patients received significantly higher than the norm (3.1-5.0 mmol / l) - from an average of 6.9 mmol / l to 7.4 mmol / l each. The most identifiable in terms of genes and genotypes was similar to the control group - the Trp / Arg genotype belonging to the ADRB3 (rs4994) Trp64Arg gene - averaging 7.4 mmol / l. A similar indicator was observed in A /
G (mean 7.1 mmol / l) and Trp / Trp genotype (mean 7.0 mmol / l) (P <0.05).

It was found that the genotypes (Trp / Arg, G / G, A / A) that determined high TMI in overweight patients (main group) were often observed even when the blood cholesterol level was high, proved to be associated with an increase in concentration. These cases were the main cause of the occurrence of CVSs in patients, such cases were interpreted as the main specific features of the distribution of gene-genotypes for patients with observed overweight.

Given the high role of high- and low-density lipoproteins (HDLP and LDLP) in overweight and obesity, a comparative analysis of their dependence on genes and genotypes of patients and individuals included in the control group was performed (Figure 3).

The figures show that the highest values in both groups were related to the G / G genotype - 3.01 mmol / l and 1.43 mmol / l (P <0.05), respectively. This situation was the same in both groups. However, in contrast, large values in patients also belonged to Trp / Trp and S / S genotypes - averaging 2.96 mmol / l and 2.97 mmol / l (P <0.05), respectively. No such significant difference was observed in the control group.

In addition, if the control group parameters were within the norm (reference quantities 0.72-1.63 mmol / l), the main group parameters differed significantly from the norm data - an average of 2.67 mmol / l to 3.01 mmol / l until. All indicators were correlated with high body mass, TMI, excess cholesterol levels in the blood, no such correlation was observed in the control group. Therefore, such dependencies in the main group were interpreted as “pathological dependencies” and dependencies in the control group as “physiological dependencies”.

CONCLUSION

Among the 7 genotypes of the 3 genes in the polymorphism of genes and genotypes in cardiovascular disease, the Trp / Trp genotype of the ADRB3 (rs4994) _Trp64Arg gene was most common in the primary and control groups, while the C / C genotype of the PPARG2 (rs1801282) _C34G gene was the most common in the control group. The ADRDB2 (rs1042713) A / G gene is less common in the A / A genotype than in the Trp / Trp and C / C genotypes. The remaining PPARG2 (rs1801282) _C34G gene G / G genotype differed relative to each other in the primary and control groups.

When the genes and genotypes of cholesterol, HDLP and LDLP in the blood of patients diagnosed with AIDS were studied, it was found that all three indicators were significantly higher than the norm in the main group, the control group data were within the norm.
Cholesterol, HDL, and LDL levels were higher in the main group before hypocaloric diet therapy than in the 7 genotypes of the three genes of CVSs.

REFERENCES:
1. Solntseva A.V., E.A. Aksenova, A.V. Sukalo, Gendernye razlichiya i geneticheskiy jinimorfizm adiponecctina u detey 2010; 221-226 [Solntseva A.V., E.A. Aksenova, A.V. Sukalo, Gendernie razlichiya i geneticheskiy polymorfizm adiponecctina u detey 2010; 221-226] [In Russ].


