was evaluated in terms of changes in the level of the main stable metabolites of nitric oxide (NO2 and NO3), in the
membranes of red blood cells in the blood plasma and in exhaled breath condensate (EBC). All the patients underwent spirometry
as well. The evaluation of the drug effectiveness was carried out before and after the treatment.

Results. It has been established that during the period of asthma exacerbation, high levels of nitric oxide in the blood,
red blood cells and EAC can be found, which is the sign of endothelial dysfunction. Interdependency between the indicators
of respiratory function (degree of obstruction) and the content of nitric oxide in the SSC has been found: the more severe
the obstruction, the higher the rates of nitrogen oxide in the SSC. The results show the positive effect of L-arginine on en-
thelial system performance and spirometry along with a basic therapy.

Conclusions. The use of L-arginine has a positive effect on the endothelial system and spirometry in patients with
asthma against pathogenic therapy.

Key words: Asthma, L-arginine, SSC, endothelial dysfunction.

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Abstract. Pro197Leu polymorphism of the gene GPX1 in 102 patients with arterial hypertension and
concomitant abdominal obesity and 97 healthy individuals have been studied. Disorders of distribution of genotype
frequencies comparing with the control group at the ex-

ience of the reduction of Pro/Pro genotype frequency have
been found in the main group. Analyzing the data, the in-
creasing risk of disorders in the GPX1 activity in patients
with Pro/Leu and Leu/Leu variants of polymorphism
comparing with homozygotes for the "wild" allele at 4,7
and 6,9 times respectively, had been revealed. Analyzing
the changes of carbohydrate metabolism depending on the

Key words: Pro197Leu polymorphism of the gene
GPX1, carbohydrate metabolism, insulin resistance,
abdominal obesity, metabolic syndrome.

Introduction. Cytoplasmic glutathione
peroxidase (GPX1) is one of the selenoenzymes
important for the organism functioning, present in all
tissues of the human body, which takes part in
detoxication of hydrogen peroxide and products of
lipid peroxidation, as it catalyzes the interaction of
reduced glutathione with these substances [3, 8, 5,
10]. Numerous pathologic processes in the organism
are known to develop as a result of disorders in the
mechanisms of antioxidant protection. In particular,
the patients with insulin resistance, accompanied by
hyperglycemia and increased production of cytokines,
acquired oxidant stress. The accumulation of free
radicals activates factors of transcription such as
NFkB, which initiate the process of proinflammatory
cytokines release[6]. The accumulation of free
radicals results in lipid peroxidation of cellular
membranes, causes atherosclerosis and endothelial
dysfunction [11]. We studied single nucleotide
polymorphism of the gene GPX1 for going into the
question of the dependence of these processes upon
the disorders of redox homeostasis. The human gene
GPX1 is localized in 3p21 chromosome and consists of
two exons. Several single nucleotide polymorphism
variants of this gene have been known, but the
Pro197Leu polymorphism has been under our study,
at which in the position 593 the amino acid cysteine
(C) is replaced with thymine (T) (C593T), resulting in
the substitution of the amino acid proline for leucine in
the 197 codon. This mutation refers to missens-
fucntional polymorphisms [1]. Pro-allele is «wild»,
while Leu- is a «mutant» allele. The presence of Leu-
allele causes depression of GPX1 sensitivity to
stimulating factors [7].

Thus, Bastaki et al. discovered that GPX1
activity 6 times slows down in homozygous patients
for the Leu-allele[3]. Zelkova T.V. et al. found out
that the homozygous for mutant allele more often

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PECULIARITIES OF CARBOHYDRATE METABOLISM OF PATIENTS WITH
ARTERIAL HYPERTENSION AGAINST THE BACKGROUND OF ABDOMINAL
OBESITY DEPENDING ON PRO197LEU POLYMORPHISM OF THE GPX1 GENE

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suffered from coronary artery disease and myocardial infarction at the age before 50 [12].

The aim of the study. To investigate the dependence of carbohydrate metabolism in patients with arterial hypertension and concomitant abdominal obesity depending on Pro197Leu polymorphism of the GPX1 gene.

Material and methods. Pro197Leu polymorphism of the gene GPX1 have been studied in 102 patients and 97 healthy individuals by isolating genomic DNA from peripheral blood leukocytes, after that amplification of the polymorphic area in the state of polymerase chain reaction (PCR) was performed on the programmed PCR thermal cyclers «Amply-4L» («Biocom», Moscow) at individual temperature response. Reagents "DNA-Absorb-B" option 100 were used for DNA isolation from lymphocytes according to instructions. PCR samples were prepared by means of the set «AmplyСенс-200-I» (Russia). Products of PCR were separated using electrophoresis in 3% agarose gel in the presence of tetraborate buffer, concentrated with ethidium bromide. Fragments were visualized by transiluminator in the presence of a marker of molecular mass 100-1000 bq (Fermentas®, USA).

Pearson's X² criterion was used to estimate the correspondence of the genotype frequencies under study to theoretically expected distribution at Hardy-Weinberg’s equation. Odds ratio (OR) with determination of 95 % confidence interval (CI) was calculated with the aim to establish the association of polymorphic variant of the gene with a pathological phenotype.

To evaluate the dependence of carbohydrate metabolism depending on Pro/Leu polymorphism of the gene GPX1 we divided the patients into groups in the following way: 18 patients with Pro/Pro, 59 with Pro/Leu and 25 with Leu/Leu genotypes, the control group consisted of 20 healthy individuals. Disorders of carbohydrate metabolism were diagnosed according to WHO criteria (1999). Fasting immunoreactive insulin (IRI), C-peptide were determined by immunoassay method, glucose content by glucose oxidase method, the content of glycated hemoglobin (HbA1c) was studied by the method of microcolumn chromatography to evaluate the compensation of carbohydrate metabolism.

To assess the degree of insulin resistance there was used small model of homeostasis (Homeostasis model assessment – HOMA [Matthew DR, 1985]). Statistical analysis of the data was carried out using the Student’s t-test and Pearson's rank correlation coefficient using the software package Statistica 6.0 for Windows. The difference was considered reliable at p<0,05.

Results and discussion. When assessing the distribution of genotype frequencies of the gene GPX1, it has been found that in the group of patients with abdominal obesity against the background of arterial hypertension there takes place a significant reduction of the frequency of Pro/Pro genotype as compared with the control group (X²=7,0, p<0,05 ), while there hasn’t been found out a reliable difference between the frequencies of Pro/Leu and Leu/Leu genotypes in the main and control groups (X²=1,9, p=0,05 and X²=2,6, p=0,05 ).

It has been revealed that Pro/Leu and Leu/Leu variants of polymorphism are associated with increased risk of violation of redox system in patients with metabolic syndrome compared with a group of healthy subjects (table 1). Thus, it has been found out that in patients with Pro/Leu polymorphism the risk of disturbance of GPX1 activity increases 5,2 times (p<0,05, OR=1,65, CI=0,95 % 0,94-2,90; table 1 ), and in patients with Leu/Leu genotype the risk of such pathology is 6,0 times higher than in persons with Pro/Pro genotype (P<0,05, OR=1,92, CI 0,95 % 0,93-3,97; table 1 ).

So, the risk of reduction of GPX 1 activity in a dose-dependent way is associated with the presence of «mutant» Leu-allele, while homozygous for the «wild» Pro-allele had significantly lower risk of this disturbance development. Pro allele has protective qualities concerning the development of redox system violation.

When studying the dependence of indices of carbohydrate metabolism on Pro197Leu polymorphism of GPX1 gene, a significantly higher level of IRI in homozygous group for the mutant allele in relation to the heterozygous group for this allele and homozygous ones for wild allele has been received, 62,8 % and 37,8 % higher respectively (p<0,05) (table 2). A credible growth of IRI in patients with Pro/Pro, Pro/Leu and Leu/Leu genotypes in relation

Table 1

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>Cases</th>
<th>Controls</th>
<th>X²</th>
<th>p</th>
<th>OR</th>
<th>0,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>102</td>
<td>97</td>
<td></td>
<td>p</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype frequency</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>Pro/Pro</td>
<td>0,176</td>
<td>0,402</td>
<td>12,91</td>
<td>0,002</td>
<td>0,32</td>
<td>0,17-0,61</td>
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<tr>
<td>Genotype frequency</td>
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<td></td>
<td></td>
<td></td>
<td>1,65</td>
<td>0,94-2,90</td>
</tr>
<tr>
<td>Pro/Leu</td>
<td>0,578</td>
<td>0,454</td>
<td></td>
<td></td>
<td>1,92</td>
<td>0,93-3,97</td>
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<tr>
<td>Genotype frequency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leu/Leu</td>
<td>0,245</td>
<td>0,144</td>
<td></td>
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</tr>
</tbody>
</table>

Note. X² - Pearson criterion, OR - odds ratio, CI - confidence interval
Table 2

Peculiarities of indicators of carbohydrate metabolism and anthropometric features in hypertensive patients with concomitant abdominal obesity according to Pro197Leu polymorphism of the gene GPX 1

<table>
<thead>
<tr>
<th>Index</th>
<th>Genotypes GPX 1, n=102</th>
<th>Control group, n=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pro/ Pro</td>
<td>Pro/ Leu</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>6,32±0,156*</td>
<td>7,49±0,112*</td>
</tr>
<tr>
<td>Immuno-reactive insulin, IU/ml</td>
<td>15,79±2,438*</td>
<td>18,64±2,362*</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>4,35±0,124***</td>
<td>4,187±0,183***</td>
</tr>
<tr>
<td>C-peptide, ng/ml</td>
<td>3,98±0,183*</td>
<td>5,23±0,149*</td>
</tr>
<tr>
<td>Leptin, ng / ml</td>
<td>16,22±4,106***</td>
<td>20,22±3,768*</td>
</tr>
<tr>
<td>HbA1C, %</td>
<td>6,55±0,326*</td>
<td>7,69±0,085*</td>
</tr>
</tbody>
</table>

Notes. 1. n - number of observations; 2. * - the probability of changes in relation to control; 3. **- the probability of changes in relation to the group with Pro / Leu-genotype; 4. ***- chance changes in relation to group with Leu / Leu genotype

The level of C-peptide in the groups with Pro/ Leu and Leu/Leu genotypes was significantly 28,9 % and 43,8 % higher respectively. The level of C-peptide in all groups of the main group, namely Pro/Pro, Pro/Leu and Leu/Leu genotypes in relation to the control group (p<0,05).

There wasn’t any reliable group difference depending on Pro/Leu polymorphism of GPX1.

Conclusions

1. In patients with arterial hypertension against the background of abdominal obesity the risk of reduction of glutathione peroxidase1 activity is associated in a dose-dependent manner with the presence of «mutant» Leu-allele, while homozygous for the «wild» Pro-allele had a significantly lower risk of this disorder.

2. The presence of Leu-allele in genotype of patients with arterial hypertension against the background of abdominal obesity is connected with the disorder of carbohydrate metabolism as a result of insulin and leptin resistance development.

Prospects for further research. The survey results indicate the necessity of development of effective measures for carbohydrate metabolism correction in hypertensive patients against the background of abdominal obesity.

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