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PLASMA HOMOCYSTEINE LEVELS AND THE FREQUENCY OF THE C677T POLYMORPHISM OF THE METHYLENETETRAHYDROFOLATE REDUCTASE GENE IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Background. The rapid global rise in the prevalence of diabetes mellitus (DM) has resulted in a corresponding increase in long-term chronic complications, which substantially diminishes work capacity and overall quality of life. Among these, diabetic neuropathy is one of the most common complications, with reported prevalence rates reaching up to 90% among patients with DM [1]. Recent studies have identified elevated levels of the amino acid homocysteine as a potential risk factor for nervous system damage [1]. Evidence from both national and international research indicates that hyperhomocysteinemia, through activation of oxidative stress mechanisms, contributes to the progression of microvascular and macrovascular complications in patients with DM.

The aim of the study – to determine plasma homocysteine levels and to evaluate the distribution of genotypes and alleles of the C677T polymorphism of the methylenetetrahydrofolate reductase (MTHFR) gene in patients with type 1 diabetes mellitus (T1DM) and chronic diabetic complications, compared with practically healthy individuals.

Research methods. A total of 84 participants were enrolled in the study and divided into two groups. Group 1: 54 patients diagnosed with T1DM and chronic complications (diabetic retinopathy, peripheral neuropathy). Group 2: 30 relatively healthy individuals without T1DM. Both groups were comparable in terms of age, sex, and body mass index. In Group 1, the mean glycated hemoglobin (HbA1c) level was 7,1%, and the mean duration of T1DM was 9,2 years. Inclusion Criteria: patients with

a confirmed diagnosis of T1DM and chronic diabetic complications (retinopathy, peripheral neuropathy), without acute concomitant illnesses.

Exclusion Criteria: patients with decompensated T1DM, severe concomitant somatic or infectious diseases in the decompensated state or acute inflammatory conditions.

Plasma homocysteine levels were measured using high-performance liquid chromatography (HPLC) with pre-column derivatization using SBD-F and fluorescence detection (Agilent 1100).

The C677T polymorphism of the MTHFR gene was genotyped using real-time polymerase chain reaction with reagents supplied by «Litekh» (Russian Federation).

Statistical analysis was conducted using Statistica 10.0, with statistical significance set at $p < 0.05$.

Results and discussion. The mean plasma homocysteine concentration in Group 1 (T1DM with complications) was 11,14 $\mu\text{mol/L}$, whereas in Group 2 (healthy controls) it was 8.09 $\mu\text{mol/L}$.

This difference was statistically significant ($p < 0.05$). In Group 1, the homozygous CC genotype was identified in 35,2% of patients, heterozygous CT genotype in 46,3%. The homozygous TT genotype of the C677T polymorphism of the MTHFR gene was found in 18,5% of patients. The frequency of occurrence of the C allele was 58.3%, and the T allele was 41,7%.

In Group 2, the homozygous genotype of CC was identified in 56,7% of patients, heterozygous CT in 36,6%. The homozygous TT genotype of the C677T polymorphism of the MTHFR gene was found in 6,7% of patients. The frequency of occurrence of the C allele was 75%, and the T allele in 25%.

A comparative analysis demonstrated a statistically significant difference between the groups in the frequency of the TT genotype ($p = 0.03$).

Conclusion. 1. Patients with type 1 diabetes mellitus and chronic diabetic complications demonstrate significantly higher plasma homocysteine levels compared with healthy individuals.

2. The prevalence of genotypes and alleles of the C677T polymorphism of the MTHFR gene was established in patients of both study groups.

3. A statistically significant intergroup difference ($p = 0.03$) was observed in the frequency of the TT genotype of the C677T MTHFR polymorphism.

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