

GENETIC AND BIOCHEMICAL DETERMINANTS OF HOMOCYSTEINE CONCENTRATION IN THE KAZAKH POPULATION

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Numerous studies have shown the role of homocysteine (HC) as a risk factor for cardiovascular disease, which plays a major role in the pathogenesis of atherogenesis and thrombus formation. A high level of HC leads to a 3-fold increase in the risk of cerebrovascular disease, and cancerogenesis.

Aim: To determine the biochemical and genetic markers of the metabolism of folic acid and homocysteine among the Kazakh population.

Material and Methods. 110 practically healthy persons (61 men and 49 women, the average age of 37.9 ± 16.1 years), Kazakh nationality were recruited to study the determinants of homocysteine concentration. All participants gave their written consent to participate in the study. The concentration of folate, vitamin B12, creatinine, albumin, total homocysteine (tHCY) in the blood was determined. Genomic DNA was isolated from blood. For the genotyping of C677T / MTHFR, the TaqMan PCR method was used. Statistical analysis was performed using the SPSS 19.0® program (SPSS, Tokyo, Japan).

Results. The level of folic acid in the blood serum in the group of Kazakh participants ranged from 0.7 to 13.5 $\mu\text{g} / \text{l}$. 72 (65.4%) of 110 had a low level of folic acid in the serum ($<3/6 \mu\text{g} / \text{l}$). The level of OGC plasma in the group of Kazakhs ranged from 5.5 to 41.1 $\mu\text{mol} / \text{l}$. Multiple regression analysis, taking into account gender and age, showed that the level of creatinine and albumin did not correlate with the concentration of HCY plasma. The level of vitamin B12 in the serum showed a relative correlation with the level of HCY ($P = 0$, $p = 0.076$). The concentration of folic acid significantly correlated with the concentration of HCY ($P = -0.26$, $p < 0.01$). The frequency of the C677T / MTHFR genotypes was 41.8% for CC, 44.5% for CT, and 13.7% for TT. The level of oocyte plasma in the Kazakhs with the TT genotype was significantly higher than in the participants in the study with the genotype CC and CT ($19.5 \pm 1.8 \mu\text{mol} / \text{l}$ vs. $9.7 \pm 0.5 \mu\text{mol} / \text{l}$, $p < 0.001$). After leveling the group by sex and age, the concentration of oGT in carriers of the TT genotype was twice as high as in the subjects with the CC and CT genotypes. Concentration of serum folate independently correlated with the level of HCY ($p = 0.007$), with the genotype of the CT of the C677T / MTHFR gene, the level of oocytes increases by a factor of 2 in comparison with the genotypes of the CC and CT. **Thus**, the determinants of hyperhomocysteinemia among the Kazakhs are the folic deficiency state, the genotype of the TT C677T / MTHFR. Effective replacement of folate levels will reduce the concentration of homocysteine. It is necessary to study polymorphisms of other genes involved in the regulation of homocysteine metabolism to identify possible additional genetic determinants of hyperhomocysteinemia