POLYMORPHISM OF ALLELIC GENES OF XENOBIOTICS DETOXIFICATION SYSTEM, HEPATOCYTES NUCLEAR CHROMATIN FUNCTIONAL STATUS IN PULMONARY TUBERCULOSIS, DEPENDING ON RESISTANCE TYPE

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Abstract

Objective — to establish allelic gene polymorphism of xenobiotics detoxification system and nuclear chromatin functional condition of hepatocytes in patients with tuberculosis (TB) depending on resistance of Mycobacteria (MBT).

Materials and methods. The study involved 100 patients with pulmonary TB and 50 apparently healthy individuals. Genomic DNA was isolated from whole venous blood. Polymorphic sites of glutathione-S-transferase (GST) were isolated by polymerase chain reaction, according to the protocol for instantaneous analysis of polymorphism by M. Arana et al (1996). Nuclear chromatin of hepatocytes was studied at 28 autopsy cases of patients deceased TB patients.

Results. A mutation in the promoter area of GST genes was revealed in 39,99 % of the patients (in 20,55 % of TB patients and in 16,44 % healthy subjects). More than half (64,81 %) of the examined were the carriers of pathological GSTM1 gene in haplotype, whereas the combination of GSTT1 homozygous mutations was 2,33 times rarer, present in almost each third (27,78 %) patient. 4,17 % of pulmonary TB patients were the carriers of the abnormal gene genotypes of both GST isoforms.

A favorable combination of functional alleles in the haplotype was characterized by less severe clinical course, less comorbidity, better treatment effectiveness in terms of partial and complete resolution of lung lesions, cavity healing, sputum smears negativation.

Conclusions. All carriers of mutant genotypes for both genes (GSTT1 0/0 / GSTM1 0/0) were treatment resistant due to the lack of enzymatic activity of detoxification system.

In drug-resistant TB mean nuclear chromatin optical density variation coefficient was higher, than in susceptible TB, indicating the imbalance between eu- and heterochromatin, reduced activity of hepatocyte nuclei and possible development of hepatic cellular dysfunction.

Key words: tuberculosis, hepatic-pancreatic-biliary system, GSTT1, GSTM1, nuclear chromatin.

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