Influence of GSTM1 and NAT2 deletion polymorphism on efficiency of TB reatment and selection of way of administration of anti-TB reparations

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ОРИГІНАЛЬНЕ ДОСЛІДЖЕННЯ

BACKGROUND. One of the important reasons of treatment falures of tuberculosis (TB) is insufficient serum concentration of anti-TB drugs in the blood of patients which contributes to the development of drug resistance strains of M. tuberculosis and the formation of multidrug-resistant tuberculosis (MDR-TB), as well as a significant number of forms resistant to isoniazid.

THE PURPOSE of the study was to assess the role of determining the type of acetylator according to the N-acetyltransferase 2 genotype and the influence of the M1 class glutathione-S-transferase gene on the efficacy of treatment for TB patients for the individual dose adjustment of anti-TB drugs and the choice of the route of administration of drugs to achieve peak serum concentrations .

MATERIAL AND METHODS. Determination of the polymorphism of the genes of the xenobiotic detoxification system, and in particular GSTM1, was carried out using the AmplisSense® GSTM1-EPh reagent set by the Multiplex Polymerase Chain Reaction (PCR) method. The genotype of acetylation was determined by allele-specific amplification of NAT2 alleles by PCR. Specific primers for wild (wt) and mutant alleles M1, M2 and M3 were used. Thus, the NAT2 polymorphism C> T 481 NAT2* 5A, G> A 590 NAT2 * 6A, G> A 857 NAT2 * 7A/B M3 was investigated.

RESULTS AND DISCUSSION. The presence of deletion of the functional zone of the polymorphic site of the GSTM1 gene increases the risk of a low efficiency of treatment for patients with pulmonary tuberculosis (in the absence of Ro-dynamics or negative Ro-dynamics) by 1.85 times [OR = 3.55, p = 0.035] and has the lowest chances on partial [OR = 0.22, p = 0.018] and complete resorption of focal-infiltrative changes in the lungs or healing of the cavity of decay after treatment [OR = 0.15, p = 0.004], accompanied by a low probability of stopping bacterial secretion by 60, 90 (for VDTB, PRTB) at doses [OR = 0.07, p = 0.002 and OR = 0.37, p = 0.04]; The 0-genotype of the GSTM1 gene is protective against the appearance of VDTB [OR = 0.37, p = 0.04 and OR = 0.22, p = 0.007]. The absence of mutation in the GSTM1 gene, on the contrary, is a risk factor for VDTB [OR = 2.67, p = 0.033], however, it increases the chances for positive Ro-dynamics under the influence of treatment with resorption (full / partial) focal-infiltrative changes, or healing of the decay cavity (1.39 and 1.44 times [OR = 4.50, p = 0.009 and OR = 6.75, p = 0.002, respectively]), increases the likelihood of a bacterial withdrawal of at least 60 doses of 1.5 times [OR = 14.06, p = 0.005].

CONCLUSIONS. Determining the concentration of isoniazid 4 hours after taking the drug can help predict the effects of TB treatment and possible correction of the treatment of the disease. In order to improve the efficacy of treatment, it is advisable to increase the therapeutic dose of isoniazid in patients with TB with the genotype of "fast acetylators" at least 7-8 mg/kg per day and the use of the parenteral route of administration.