

## THE EFFECTIVENESS OF TREATMENT OF PULMONARY TUBERCULOSIS DEPENDING ON CYP3A4 GENOTYPE

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Abstract

Among the factors that can influence the course and effectiveness of the treatment of pulmonary tuberculosis (TB) the genetic characteristics of patients play an important role. It is established that cytochrome (CYP) 3A4/5 is involved in metabolism of more than 30 % of xenobiotics. Consequently, the activity of this enzyme is greatly influenced by responsible genes, such as CYP3A4.

*The aim of the study* was the investigation of prognostic value of CYP3A4 polymorphism on the course and effectiveness of anti-tuberculosis therapy in patients with pulmonary TB.

*Materials and methods.* Using PCR method, a detection of polymorphism of CYP3A4\*1B, CYP3A4\*1G genes, which determine the activity of CYP3A4 enzyme, was performed in 105 patients with newly diagnosed pulmonary TB. We have reviewed medical records at the beginning and at the end of inpatient treatment and considered the form, extent, regression rate of TB-lesions, and the rate of smear-positive cases. A statistical analysis of study data, expressed in absolute or relative values, was done using Pearson's chi-squared test.

*Results:* It was established that out of 105 enrolled TB-patients 84 individuals (80,0%) carried the genotype of "rapid metabolizers" (RA), the rest – 15 (14,3%) and 6 (5,7%) individuals were "intermediate metabolizers" (IM) and "slow metabolizers" (SM) correspondently. According to CYP3A4 genotype in patients with SM and IM the bi-lateral lesions as well as the processes of pulmonary destruction and dissemination, as well as smear-positiveness occurred more frequently than in RM. For example, in IM group the dissemination was observed almost two times more frequently than in RM ( $P < 0,05$ ;  $\chi^2 = 4,44$ ). At the end of the in-patient treatment in SM remaining TB-infiltrates observed more often, while the resolution of consolidation registered more rarely (66,7%) than in IM and RM (81,0% and 80,0%, correspondently). Also, in SM the TB infiltrates remained more often than in RM (33,3% versus 8,3%,  $P < 0,05$ ;  $\chi^2 = 4,44$ ). At the same time in IM the smear-positive status remained more often than in other groups.

*Conclusion.* Genotypes of "intermediate metabolizers" and "slow metabolizers" according to CYP3A4 genes were associated with unfavorable pulmonary disease both at initiation and at the end of in-patient phase of the TB treatment. Identification of CYP3A4 genotype in pulmonary TB patients allows allocation of the groups of high risk of unfavorable TB course.

**Key words:** pulmonary tuberculosis, CYP3A4 gene polymorphism, treatment, effectiveness, prognosis.