

# PHARMACOKINETICS OF ISONIAZID IN TUBERCULOSIS PATIENTS WITH DIFFERENT ACETYLATION GENOTYPE

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## *Abstract*

Lower concentration of anti-tuberculosis drugs in patient's organism could be one of the causes of insufficient effectiveness of chemotherapy of pulmonary tuberculosis. Accordingly, the aim of current study was to determine isoniazid concentration in tuberculosis (TB) patients considering their acetylation genotype.

NAT2 (N-acetyltransferase 2) polymorphisms C>T 481 NAT2\*5A, G>A 590 NAT2\*6A, G>A 857 NAT2\*7A/B was analyzed using polymerase chain reaction (PCR) technique. Isoniazid concentration was measured in venous blood 2, 4, 6 and 24 hrs after oral administration of standard dose according to Vollenberg method in modification of R. I. Shenderova using spectrophotometer.  $T_{1/2}$  (half-life), AUC (area under curve), MRT (mean residence time) of isoniazid were calculated. The blood samples were obtained from newly diagnosed TB patients, admitted to Odessa regional tuberculosis dispensary in 2012.

Among 84 patients according to NAT2 genotype 39,3 % of individuals belonged to fast or intermediate acetylators, others — 60,7 % — to slow acetylators. In fast/intermediate acetylators the isoniazid concentration 4 and 6 h after isoniazid administration was correspondently 20,6 % and 38,0 % less, than in slow acetylators. In about 20 % TB patients, irrespectively of acetylation genotype, 2 and 4 h after drug administration isoniazid concentration was below minimal inhibitory concentration for mycobacteria (< 3 and < 1,5 mcg/ml respectively). In fast/intermediate acetylators low blood 6 h post-dose concentration of isoniazid was observed two times more frequently than in slow acetylators (42,4 % versus 19,6 %). The half-life of isoniazid in fast/intermediate acetylators in all control points was lower, than in slow acetylators. This data have demonstrated an important difference in pharmacokinetics of isoniazid in TB-patients with different acetylation genotype.

**Key words:** tuberculosis, acetylation genotype, isoniazid.

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