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Genetic polymorphisms in metabolic enzymes and susceptibility to anti-tuberculosis drug-induced hepatic injury

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ABSTRACT. We examined the relationships between *N*-transacetylase 2 (NAT2), cytochrome P450 (CYP) 2E1 enzyme, glutathione *S*-transferase M1, T1 (GSTM1/GSTT1) gene polymorphisms, and anti-tuberculosis drug-induced hepatic injury (ADIH). A one-to-one matched case-control study was carried out using clinical data. *NAT2*, *CYP2E1*, *GSTM1*, and *GSTT1* polymorphisms were identified in 173 pairs of research subjects. Statistical analysis was performed to determine risk factors of ADIH. The results showed that low body mass index and alcohol consumption were risk factors of ADIH, with odds ratios of 6.852 and 3.203, respectively. The frequencies of *NAT2* slow acetylator, *CYP2E1* -1259G>C, -1019C>T wild-type, and the *GSTM1* null genotype were higher in the case group than in the control group, with odds ratios of 2.260, 2.696, 4.714, and 2.440, respectively. *GSTT1* was not found to be related to ADIH. Interactive analysis showed that *NAT2* slow acetylator and the *GSTM1* null genotype were mutually synergistic, while an antagonistic relationship was observed between

the *CYP2E1* wild-type genotype and the other 3 genetic types. The risks of hepatic injury were higher after anti-tuberculosis therapy in patients carrying the *NAT2* slow acetylator, *CYP2E1* -1259G>C, -1019C>T wild-type, and *GSTM1* null genotype.

Key words: Anti-tuberculosis drug-induced hepatic injury; Tuberculosis; Anti-tuberculosis therapy; Gene polymorphism; Metabolic enzyme

