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

F.M. Feng¹, M. Guo¹, Y. Chen¹, S.M. Li², P. Zhang², S.F. Sun³ and G.S. Zhang¹

¹Key Laboratory of Occupational Health and Safety, School of Public Health, Hebei United University, Tangshan, China
²Tanshan Tuberculosis Hospital, Tangshan, China
³College of Nursing and Rehabilitation, Hebei United University, Tangshan, China

Corresponding author: F.M. Feng
E-mail: fm_feng@sina.com

Received October 16, 2013
Accepted September 18, 2014
Published November 11, 2014
DOI http://dx.doi.org/10.4238/2014.November.11.11

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