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Genetic Polymorphisms of CYP2E1 and GSTM1 Loci and Susceptibility to Anti-Tuberculosis Drug-Induced Hepatotoxicity

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Abstract

Background: Host genetic factors that influence predisposition to anti-tuberculosis drug-induced hepatotoxicity (DIH) are not clear in the Indian population.

Objective: To investigate the possible association of DIH with polymorphism at the RsaI site of the 5-prime untranslated region of CYP2E1 and GSTM1 'null' mutations.

Methods: In this prospective study, 113 tuberculosis (TB) patients with DIH and 201 TB patients receiving anti-tuberculosis treatment without developing hepatotoxicity (non-DIH) constituted cases and controls, respectively. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was performed to analyse genetic polymorphisms of CYP450 2E1 at the RsaI site and 'null' GSTM1 mutations. PCR-RFLP results were compared between 185 non-DIH and 105 DIH patients

Results: A high frequency of c1c1 genotypes of CYP2E1 was commonly encountered, and the difference between DIH and non-DIH patients was not significant (75.14% vs. 77.14%). The genotypic distribution of c2c2 was significantly higher in the DIH than in the non-DIH group (4.8% vs. 0.5%, OR 8.58, P = 0.03). However, adjustment for age, sex and serum albumin differences yielded an OR of 2.75, making it non-significant (P = 0.26). Homozygous 'null' mutation frequencies at the GSTM1 gene in DIH and non-DIH patients were observed that were not significantly different (40% and 37%, respectively, P = 0.61).

Conclusion: RsaI variants of the CYP2E1 gene and GSTM1 'null' mutation were not associated with risk of DIH in a north Indian population.