

P17 UDP-GLUCURONOSYL-TRANSFERASE 1A1 POLYMORPHISMS (UGT1A1*28) IN THAI β -THALASSEMIA/Hb E AND HEALTHY VOLUNTEERS: RELATIONSHIPS TO JAUNDICE AND GALLSTONE FORMATION

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The UDP-glucuronosyltransferases (UGTs) are important Phase II metabolizing enzymes. These enzymes play a critical role in hepatic metabolism of a variety of endogenous and exogenous compounds, including bilirubin steriods and drugs. Genetic polymorphisms or variants of different isoforms may be associated with disease states or even abnormal drug metabolism. A promoter polymorphism of UGT1A1 (UGT1A1*28) is associated with Gilbert's Syndrome, a deficiency in bilirubin glucuronidation leading to mild hyperbilirubinemia. Chronic hyperbilirubinemia and gallstone are unusually common in people with thalassemia/Hb E. To determine whether this has a genetic basis in this population we compared the bilirubin levels and frequency of gallstones in both thalassemic and normal subjects with different alleles of the UGT1A1 promoter gene. This communication describes data on genetic UGT1A polymorphisms in 330 Thai β -thalassemia/HbE and 42 normal subjects. Genomic DNA was obtained by standard methods from peripheral blood leukocytes. The (TA)_n promoter polymorphism of UGT1A1 was analyzed by size using an ABI 310® genetic analyzer. The frequencies of the 6/6, 6/7, and 7/7 UGT1A1 promoter genotypes in thalassemic subjects were 0.72, 0.25, and 0.02, while the frequencies in normal subjects were 0.69, 0.31, and 0.0, respectively. Each of the polymorphism of UGT1A1 were separately tested for agreement with assumption of Hardy-Weinberg equilibrium. There was a significantly higher total bilirubin level in those with the 7/7 and 6/7 genotype compared with 6/6 genotype ($p=0.02$ and $p=0.03$). But no significant difference was found between total bilirubin level of patients with 6/7 and 7/7 genotype ($p=0.07$). The decrease of the ratio of direct bilirubin to total bilirubin affected by genetic of UGT1A1 were higher in normal subjects than in thalassemia. The patients with 7/7 genotype appeared more prone to gallstone formation (100%) than those with 6/7 (47%) and 6/6 (41%) genotype. These results suggested that genetic polymorphisms in the key UGT1A enzyme family influence on serum bilirubin level in both groups of subjects. However the high incidence of gallstones in patients with 6/7 and 6/6 genotypes could be caused by other factor such as other site of mutation, food, environmental factors or pathophysiology in the patients.