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Pharmacogenetics of uridine diphosphoglucuronosyltransferase (ugt 1a6) and its role in patient response to deferiprone

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Abstract

This study was planned to find UGT1A6 polymorphisms (SNPs) and evaluate its effect on metabolism of deferiprone to deferiprone glucuronide in thalassemic patients. The concentrations of deferiprone and deferiprone glucuronide were determined by high performance liquid chromatography. The UGT1A6 genotype was studied through sequence polymorphisms in exon 1 of the gene using restriction fragment length polymorphism after PCR amplification. All the hematological and biochemical parameters of patients deviated from normal values. The concentration of deferiprone and deferiprone glucuronide in plasma after 3 h of drug administration was 2.35 µg/mL and 3.60 µg/mL, respectively in all thalassemic patients. The concentration of deferiprone in pooled urine (0-12 h) was 10.3 µg/mL and 103.10 µg/mL, respectively. The total amount of deferiprone excreted through urine in 12 h was 2.46 mg and was 0.26% of the dose. The deferiprone glucuronide excreted through urine in 12 h was 26.51 mg which was 2.86% of the administered dose. UGT1A6 polymorphisms for T181A and R184S were found in eight different combinations. UGT1A6 homozygous was the most common genotype and was 50 % of the total thalassemic patients. The maximum concentration of DFP and DFP-G in plasma was found in GT 32 and GT 11. The difference in concentration of DFP-G in plasma is highly significant among the eight genotypes. Therefore, the study suggests that patient should be genotype before iron chelation with deferiprone.

Biography

Abdul Ghaffar has completed his PhD in Biotechnology in 2009 from Quaid-i-Azam University, Islamabad, Pakistan. Dr. Ghaffar started his professional carrier in 2004 as lecturer and was later promoted as assistant professor at University of Agriculture, Faisalabad, Pakistan. He joined Government College University, Faisalabad in 2011. He has published 5 papers in internationally reputed journals and is member of review committee of Journal of Molecular Biology Reports and Journal of Chemical Society of Pakistan