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Study of CYP3A4 and UGT1A1 polymorphisms in chronic myeloid leukemia patients administered nilotinib and relation to hyperbilirubinemia

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UGT1A1 is the sole enzyme responsible for bilirubin metabolism. Its polymorphic form, UGT1A1*28, results in decrease of its activity. Hyperbilirubinemia is one of the common laboratory abnormalities found in Ph+ve chronic myeloid leukemia (CML) patients administered with the 2nd generation tyrosine kinase inhibitor 'nilotinib'. Studies supported that the inhibitory effect of nilotinib on UGT1A1 contributed to hyperbilirubinemia and was more increased with patients having UGT1A1*28. About 30% of the given dose of nilotinib is metabolized primarily with CYP3A4. CYP3A4*1B may affect response and toxicity through changing the enzyme activity. This research aimed to study these genes' polymorphisms and relate them to the bilirubin toxicity. DNA was isolated from blood samples collected from 43 Egyptian CML patients administered nilotinib at National Cancer Institute (NCI). High resolution melting technique (HRM) was used for the detection of the polymorphisms. Bilirubin levels were analyzed pre- and post-treatment. Wild type for UGT1A1 and CY P3A4 were observed in 78% and 86%, respectively. Grade 0 toxicity was observed in 68%, 18% grade I, 12% grade II and 2% grade III. Hyperbilirubinemia was not significantly correlated with UGT1A1 polymorphism or with CYP3A4 and UGT1A1 polymorphisms. However, larger sample size is needed to confirm the results as the prospective genotyping of these genes can lead to personalized treatment.

Biography

Shaimaa Ahmed Mohamed Ahmed Fahmy is a Research Pharmacist at the Biochemistry Unit, Cancer Biology Dep., National Cancer Institute, Cairo University, Egypt since 2013. She is also a Master's degree candidate of Pharmacology and Toxicology at Faculty of Pharmacy, Cairo University, since 2013. She graduated from Faculty of Pharmacy, Cairo University in 2012 and joined the Research Department of the Children Cancer Hospital, Egypt. She has one ongoing unpublished article and she currently joined a grant project on HCC and drug resistance. She has special interest in pharmacogenomics and personalized medicine.

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