Evaluation of CYP1A2 Activity in Thalassemia Patients

Veerapol Kukongviriyapan, Laddawan Senggunprai, Upa Kukongviriyapan[1], Arunee Jetsrisuparb[2], Wichittra Tassaneyakul

Departments of Pharmacology, [1]Physiology and [2]Paediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Abstract

The thalassemias are common genetic diseases among the Thai population. The autooxidation of globin chains and iron overload are the suggested mechanisms for the enhanced generation of reactive oxygen species and ensuing oxidative stress. It has been reported that the oxidative stress alters function of the drug metabolizing enzymes system. However, several cellular adaptive compensations against oxidative stress may modify the outcome of the activity of the enzymes. The aim of this study was to evaluate the drug metabolizing enzyme status in thalassemia patients, particularly to examine the activity of CYP1A2, and to determine factors influencing its activity. The study included the regular blood transfusion β-thalassemia / HbE patients (n = 23) and the healthy controls (n = 25). The CYP1A2 activity was assessed by using caffeine as a probe drug. The caffeine and its major metabolite, paraxanthine, in saliva and plasma at 6 h after drug intake, were analyzed by high performance liquid chromatography (HPLC). The enzyme activity was determined from the caffeine metabolic ratio (CMR), paraxanthine / caffeine. The oxidative status was quantified by measuring the concentrations of plasma and whole blood total glutathione. Moreover, the concentrations of hemoglobin, uric acid, total bilirubin, ALT and AST were analysed in both groups. The results showed that the salivary CMR highly correlated with the plasma CMR ($r = 0.9772$, $p = 0.0001$). The salivary and plasma CMR in thalassemia patients were not significantly different in comparison with the control group (plasma CMR : 0.759 ± 0.043 vs 0.775 ± 0.062 for control group and thalassemia patients, respectively). Similarly, there was no significant difference between the two groups in the concentrations of plasma total glutathione, whereas, the whole blood total glutathione was significantly decreased in thalassemia patients ($p < 0.05$). Correlations between parameters were analysed by using multiple linear regression analysis. In the control group, none of the parameters correlated with the CMRs. In contrast, the plasma CMR correlated significantly with the concentrations of total glutathione, total bilirubin, ALT and AST in the thalassemia patients ($r = 0.65$, $p < 0.05$). In conclusion the CYP1A2 activity in thalassemia patients was not significantly altered and its activity in these patients may be affected by the oxidative stress responses.

Keywords : thalassemia, CYP1A2, caffeine, oxidative stress