บทคัดย่อ

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Evaluation of drug metabolizing enzyme status in thalassemia patients

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The alpha thalassemia, beta thalassemia and hemoglobin (Hb) variant E are common in Thai population. The autooxidation of globin chains and iron overload are the suggested mechanisms for the enhanced generation of reactive oxygen species ensuing oxidative stress. Moreover, iron overload in the liver results in an impairment of liver function. It has been reported that the oxidative stress alters function of the drug metabolizing enzyme system. However, several cellular adaptive compensations against oxidative stress may modify the outcome of the stress response. The aim of this study was to evaluate the drug metabolizing enzyme status in thalassemia patients, particularly to examine the activities of CYP1A2 and CYP3A4, and to determine factors influencing their activities. The study included the regular blood transfusion β-thalassemia/HbE patients (n=24) and the healthy controls (n=25) with (mean ± SE) 11 ± 0.3 and 12 ± 0.6 years of age, respectively. The CYP1A2 and CYP3A4 activities were assessed by using *in vivo* test probes, caffeine and dextromethorphan, respectively. The salivary and plasma caffeine metabolic ratio (CMR) (paraxanthine / caffeine), obtained at 6 h after caffeine intake were used for assessing the CYP1A2 activity. The CYP3A4 activity was determined from the 3-methoxymorphinan (3MM) / dextromethorphan (DM) ratio in urine sample taken over the time period of 4-6 h after taking dextromethorphan. The oxidative status was quantified by measuring the concentrations of total sulfhydryl groups and total glutathione in plasma and whole blood. The laboratory examinations including complete blood count, serum ferritin level, liver function test and viral hepatitis B detection were performed in both groups. A significant decrease in the concentrations of total sulfhydryl groups and total glutathione in whole blood was shown in thalassemia patients, indicating a diminution of total antioxidant capacity in these patients ($p < 0.05$). In assessment of CYP activities, the plasma and salivary CMR and the urinary 3MM / DM ratio were not significantly different from those of control (plasma CMR: 0.76 ± 0.04 vs 0.75 ± 0.06 and 3MM / DM ratio: 0.33 ± 0.07 vs 0.24 ± 0.04 for control and thalassemia patients, respectively). However, splenectomized thalassemia subjects showed a significant decrease in the 3MM / DM ratio when compared with the non-splenectomized patients (0.13 ± 0.04 vs 0.30 ± 0.04, $p < 0.05$, respectively). In the thalassemia patients, there were no correlation between plasma CMR and any physiologic and oxidatant status parameters, likewise, none of these parameters were associated with the 3MM / DM ratio. In conclusion, the CYP1A2 activity was not significantly altered in thalassemia patients who are in stable condition. Activity of CYP3A4 was apparently decreased in splenectomized patients and this may be associated with an abnormal liver function in these patients.