MTR-1 and CYP450 gene polymorphisms and 12-hour AUC pharmacokinetics of tacrolimus

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Background: To study whether and how gene polymorphisms of the P-glycoprotein system (MTR=1) and cytochrome P450 enzyme system (CYP3A4 and CYP3A5) affect the oral pharmacokinetics of tacrolimus (Tac). Data on trough level (C0) shows that CYP3A4 but not MTR-1 polymorphism, influences the dose normalized (dn) C0. However, no information exists on the relationship of polymorphisms in these systems and the oral bioavailability (AUC), Cmax and Tmax. Methods: In 38 renal transplant recipients with a stable Tac C0, a 12-hour time-concentration profile of Tac was performed. Influence of polymorphisms of MDR-1 (CTT/CTT), CYP3A4 (AA/AG/GG) and CYP3A5 (AA/AG/GG) on the dn AUC, Cmax, Tmax and C0 was analyzed by non-parametric statistics (Kruskal-Wallis). Results: Concerning MDR-1 gene, the respective median values of dnAUC (ng*h/mL per mg/kg), Cmax (ng/mL), Tmax (hr) and dnC0 (ng/mL per mg/kg) were 1333.1, 33.0, 1.0 and 55.19 for CC genotype (n=9), 2224.0, 38.5, 1.0 and 174.24 for CT genotype (n=11), 1807.8, 68.0, 1.0 and 99.00 for TT genotype (n=11). Differences of these parameters were not significant. For CYP3A4/3A5 gene, the respective median values of dnAUC (ng*h/mL per mg/kg), Cmax (ng/mL), Tmax (hr) and dnC0 (ng/mL per mg/kg) were 1966.0, 37.6, 1.0 for AA, 713.0, 3.9, 1.0 for AG and 1167.1, 6.1, 1.0 and 53.28 for AA–GG genotype (n=22). The p value was < 0.01 in dnAUC and dnC0 but not significant in Cmax or Tmax. Conclusions: Polymorphisms of the CYP genes are related to differences in AUC but not in Cmax or Tmax. MTR-1 gene polymorphism has no significant relationship in tested parameters.

A single center study of tuberculous peritonitis complicating continuous ambulatory peritoneal dialysis in Hong Kong

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Background: Tuberculous peritonitis (TBP) was generally regarded as a rare complication of continuous ambulatory peritoneal dialysis (CAPD). However, it was found to be an uncommon complication of Chinese CAPD patients in Hong Kong. Methods: This is a one-year retrospective single center study of the treatment and outcome of TBP complicating CAPD. Nine cases of TBP were identified in our 596 patients receiving CAPD between 1st January 2003 and 31st December 2003. All of them were diagnosed by positive acid-fast bacilli culture. Results: There were three male and six female patients. Four of them had diabetes mellitus while one had carcinoma of the cervix treated by radiotherapy. None of them had a past history of tuberculosis. Extraperitoneal tuberculosis was not observed. There was no concurrent bacterial peritonitis. All patients showed neutrophil predominance in the peritoneal fluid (PDF). None of them had a past history of tuberculosis. There was no concurrent bacterial peritonitis. All patients showed neutrophil predominance in the peritoneal fluid (PDF). The p value was < 0.01 in dnAUC and dnC0 but not significant in Cmax or Tmax. Conclusions: Polymorphisms of the CYP genes are related to differences in AUC but not in Cmax or Tmax. MTR-1 gene polymorphism has no significant relationship in tested parameters.

Hypokalemia in Chinese peritoneal dialysis patients: prevalence and implications

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Aim: Abnormal potassium metabolism may contribute to the increased cardiac morbidity and mortality seen in dialysis patients. We studied the pattern of abnormal potassium metabolism in a cohort of Chinese peritoneal dialysis patients. Methods: We reviewed the serum potassium levels of 266 PD patients during 3 consecutive clinic follow-ups. Results: One hundred and thirty five patients (50.8%) were male and thirty five patients (50.8%) were female. The mean age was 52.3 years. Mean duration of dialysis was 38.1 ± 28.9 months. The mean serum potassium level was 3.9 ± 0.5 mmol/L. Five patients (1.9%) had an average serum potassium level < 3.5 mmol/L. Conclusions: Forty-six (17.3%) and 140 (52.6%) patients had one or more serum potassium levels below 3 mmol/L and 3.5 mmol/L, respectively. In addition, another 21 patients (7.9%) required potassium replacement. Kav had a significant negative correlation with Charlson’s Comorbidity Index (r = -0.155, p = 0.01). Kav had a significant correlation with the overall Subjective Global Assessment score (r = 0.276, p < 0.01) and serum albumin level (r = 0.173, p < 0.01). There was no correlation between Kav and the daily PD exchange volume, ultrafiltration volume, or KT/V. There was also no correlation between Kav and urine volume or residual glomerular filtration rate. Conclusions: Persistent and intermittent hypokalemia are common in Chinese PD patients. The serum potassium level in PD patients may reflect the nutritional status or the severity of coexisting comorbid condition. Further studies may be needed to investigate the long term significance of hypokalemia in PD patients.