Poster

[P27-10] P27-10: Pharmacokinetics and pharmacogenetics

Chair: Andrew Somogyi, Australia

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[P27-10-7] Phenoconversion of CYP3A in chronic renal failure; what is the factor involved?

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Background

Cytochrome P450 (CYP)3A is the most important enzyme involved in the metabolism of 30-40% of currently prescribed drugs. Phenoconversion is a phenomenon by which the metabolic activity in extensive metabolizer decreases to the same degree as that in poor metabolizer. Renal failure has been reported to decrease CYP3A activity *in vivo*, but whether phenoconversion of CYP3A occurs in patients with renal failure is unknown. The aim of this study was to identify the factor associated with phenoconversion of CYP3A in patients with chronic renal failure, by measuring plasma concentration of 4β-hydroxycholesterol as an endogenous marker for CYP3A.

Methods

Sixty-three stable kidney transplant recipients who underwent transplantation more than 180 days prior to the study were recruited. They comprised 23 recipients with *CYP3A5*1* allele (*CYP3A5*1/*1* or **1/*3*) and 40 recipients without *CYP3A5*1* allele (*CYP3A5*3/*3*). Morning blood samples were collected, and plasma concentrations of 4β-hydroxycholesterol, indoxyl sulfate, intact parathyroid hormone (PTH), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) were measured.

Results

Plasma concentrations of 4β-hydroxycholesterol in recipients with *CYP3A5*1* allele were significantly higher than those in recipients without *CYP3A5*1* allele and the cut-off value between two groups was 40 ng/mL. Ten of 23 recipients with *CYP3A5*1* allele showed phenoconversion, with plasma 4β-hydroxycholesterol concentrations lower than 40 ng/mL. Recipients with phenoconversion (n = 10) had significantly higher plasma indoxyl sulfate concentrations than recipients without phenoconversion (n = 13), but the two groups did not differ significantly in intact PTH, IL-6 or TNF-α.

Conclusions

This study suggests that phenoconversion of CYP3A occurs in patients with chronic renal failure and indoxyl sulfate may be involved in the phenoconversion induced by renal failure.