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Benefits of minimizing immunosuppressive dosage according to cytochrome P450 3A5 genotype in liver transplant patients: findings from a single-center study

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ABSTRACT. We evaluated the clinical efficacy of tailoring tacrolimus dosage to cytochrome P450 (CYP) 3A5 genotype in liver transplant patients. One hundred patients who received tacrolimus-based therapy were included in the retrospective study in which the relationship between the tacrolimus blood trough concentration/dosage ratio and the CYP3A5 genotype of both donors and recipients was determined. Subsequently, 106 patients were continuously enrolled in a prospective study and followed-up for 6 months; the relationship between tacrolimus dosage and CYP3A5 genotype was also determined. Rates of acute rejection, hepatotoxicity, renal toxicity, neurotoxicity, hypertension, and hyperglycemia were compared between the groups. During the 6 months following liver transplantation, the mean tacrolimus concentration/dosage ratio among patients who did not have the CYP3A5*1 genotype and who received a transplant from a

donor with the same genotype (24/100, 24% of patients) was higher than that among patients who did have the CYP3A5*1 genotype and/or had a donor with the same genotype (76/100, 76% of patients). In the second part of the study, the tacrolimus dosage was tailored to CYP3A5 genotype and 24 patients (22.64%) received a lower dose. There was an obvious decrease in acute rejection, hepatotoxicity, renal toxicity, neurotoxicity, hypertension, hyperglycemia, and *Pneumocystis carinii* infection among the latter group. A lower tacrolimus dose was suitable for about 25% of the liver transplant patients, as these patients did not have the CYP3A5*1 genotype and received a transplant from a donor with the same genotype. Tailoring the tacrolimus dosage according to the CYP3A5 genotype could reduce rejection and adverse effects.

Key words: Cytochrome P450 3A5; Liver transplantation; Tacrolimus; Transplant rejection; Renal toxicity

