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한국인 신이식환자에서 CYP3A와 ABCB1 다형성이 용량 보정 타크로리무스 trough level에 미치는 영향

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조장희, 진미경, 권오언, 홍경득, 권소연, 안지선, 오세현, 최지영, 윤세희, 박선희, 김용림, 김찬덕

Impact of CYP3A and ABCB1 Polymorphisms on Tacrolimus Dose-adjusted Trough Levels Among Renal Transplant Recipients in Korea

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Background: Tacrolimus is a substrate of cytochrome P450 3A (CYP3A) and P-glycoprotein (P-gp), encoded by the CYP3A and ATP-binding cassette sub-family B member 1 (ABCB1) genes, respectively. This study was aimed to investigate the impact of CYP3A and ABCB1 polymorphisms on the tacrolimus pharmacokinetics and clinical outcomes in renal transplant recipients in Korea.

Methods: We retrospectively analyzed data from a cohort of 63 renal transplant recipients receiving tacrolimus. CYP3A4*4, CYP3A4*5, CYP3A4*18, CYP3A5*3, ABCB1 C1236>T, ABCB1 G2677>T/A and ABCB1 C3435>T polymorphisms were genotyped and correlated to dose-adjusted tacrolimus trough concentration on month 1, 3, 6 and 12 after transplantation.

Results: Frequencies of variant alleles among the renal transplant recipients were CYP3A4*4 0.0%, CYP3A4*5 0.0%, CYP3A4*18 1.8%, CYP3A5*3 77.0%, ABCB1 C1236>T 60.3%, ABCB1 G2677>T/A 57.1% and ABCB1 C3435>T 34.1%. Patients with the CYP3A5*3 alleles showed higher dose-adjusted tacrolimus concentrations for 12 months and higher trough levels until 6 month after transplantation. ABCB1 polymorphisms were not associated with tacrolimus concentrations. In a multivariate analysis, the presence of at least one CYP3A5*3 allele was significant independent variable affecting dose-adjusted tacrolimus concentrations. Glomerular filtration rate (GFR), acute rejection and opportunistic infection were not affected by CYP3A5 polymorphisms. CNI toxicity which showed higher tendency in patients with CYP3A5 *1 alleles, might be associated with higher tacrolimus dose/kg.

Conclusion: The CYP3A5 genotype is a major factor in determining the dose requirement for tacrolimus, and genotyping may be of value in individualization of immunosuppressive drug therapy for renal transplant patients.

Key Words: 타크로리무스, 약동학, 유전자 다형성
Tacrolimus, Pharmacokinetics, Polymorphisms