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타크로리무스 농도의 변동성과 평균이 이식신 성적에 미치는 영향

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Impact of Tacrolimus Variability and CYP3A5 Genetic Polymorphism on Renal Allograft Outcomes

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Background: Wide variation in tacrolimus levels and low tacrolimus exposure were reported to be associated with poor renal graft outcomes. CYP3A5 polymorphism is a representative genetic factor that might affect this association together with environmental factors. We investigated whether the tacrolimus variability or the mean tacrolimus trough level can influence kidney allograft outcomes, and whether CYP3A5 polymorphism can affect this relationship.

Methods: A total of 266 renal transplant patients (January 1, 1996-December, 31 2009) were enrolled. The tacrolimus coefficient of variation (CCV) and the mean tacrolimus trough level were calculated from the tacrolimus levels between 6 and 12 months after transplantation. The genotypes of the CYP3A5 gene polymorphism (rs776746) were determined using the TaqMan allelic discrimination assay.

Results: Neither the tacrolimus CCV nor mean trough level was associated with post-transplant 1-year eGFR. Patients with minor homozygote of CYP3A5 genetic polymorphism have lower mean tacrolimus trough level (6.70±1.84 vs 7.96±2.01 ng/mL, p=0.007) and lower post-transplant one-year estimated glomerular filtration rate (eGFR, 57.1±13.7 vs 66.2±17.0 mL/min, p=0.021). However, the tacrolimus CCV was not correlated with the CYP3A5 polymorphism. When both the tacrolimus CCV and the mean tacrolimus trough level were stratified according to CYP3A5 polymorphism, they were not associated with renal allograft outcomes.

Conclusion: CYP3A5 polymorphism was associated with the mean tacrolimus trough level and renal allograft outcomes. However, the variability of tacrolimus trough levels was not associated with the CYP3A5 polymophism and did not have a significant impact on renal allograft outcomes.

Key Words: CYP3A5, 타크로리무스, 신장이식
Tacrolimus, CYP3A5, Kidney Transplantation