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세포내 면역억제제 농도 측정 기술 개발과 임상 적용

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Monitoring Intracellular Tacrolimus Concentration in Kidney Transplant Recipients with Stable Graft Function

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Background: Monitoring the intracellular concentrations of immunosuppressive agents can be a promising approach to improve and individualize the clinical practice in patients undergoing transplantation. However, the utility of monitoring intracellular tacrolimus level in kidney transplant recipients remains unresolved.

Methods: Both whole blood and intracellular concentrations of tacrolimus (WB-TAC and IC-TAC, respectively) were measured simultaneously in 213 kidney recipients with stable graft function using LC-MS/MS. The tacrolimus ratio was defined as the ratio between IC-TAC and WB-TAC (IC-TAC/WB-TAC). In addition, the genetic polymorphisms of the ATP-binding cassette subfamily B member 1 (*ABCB1*), including rs1128503, rs2032582, and rs1045642, were examined. Flow cytometry was used to determine the proportion of T cells producing interferon gamma or interleukin 2 according to IC-TAC levels (Fig. 1).

Results: The levels of WB-TAC, IC-TAC, and the tacrolimus ratio were 4.6±1.83 ng/mL, 43.4±30.10 pg/10^6 cells, and 9.3±4.25, respectively. The correlation coefficient (r) between WB-TAC and IC-TAC was 0.67 ($p<0.001$). Genetic polymorphisms of *ABCB1* were not associated with either IC-TAC or the tacrolimus ratio. Among baseline covariates, sex, hematocrit and the transplant duration were significant predictors of the tacrolimus ratio: a high tacrolimus ratio was present in females, in patients with a low hematocrit, or in an early transplant period. After stimulation with PMA and ionomycin, the proportion of T cells producing interferon gamma or interleukin 2 was higher in the group with lower IC-TAC levels.

Conclusions: This is the first study to identify factors associated with the ratio between blood and intracellular tacrolimus levels in kidney transplant recipients. Results from this study will be helpful in monitoring and predicting intracellular tacrolimus concentrations.

Key Words: 타크로리무스, 신장 이식, 농도
Tacrolimus, Kidney transplantation, Concentration