

Analytic Validation of PETINIA Assay for Therapeutic Drug Monitoring of Mycophenolic Acid in Kidney Transplant Recipients Compared with Liquid Chromatography-mass Spectrometry

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Background: Therapeutic drug monitoring of mycophenolic acid (MPA) is required to optimize immunosuppressive effect and minimized toxicity. This study validated a new particle enhanced turbidimetric inhibition immunoassay (PETINIA) assay for determination of MPA and evaluated relationship of MPA trough level with drug-related adverse events.

Methods: A total of 54 kidney transplant recipients (KTRs) determined MPA concentrations prior to administration of the morning MPA using PETINIA and liquid chromatography-mass spectrometry (LC-MS) assay. Agreement between PETINIA and LC-MS assay was assessed by the Passing-Bablok regression and Bland-Altman plot method. Adverse events were collected from all KTRs who maintained the dosage of MPA for at least 6 month after the measurement. The association of adverse events with MPA trough level obtained by PETINIA assay was analyzed.

Results: PETINIA assay revealed a good degree of agreement with LC-MS method: Regression analysis gave an equation of $y=1.273x-0.119$ ($r=0.996$, $p<0.001$). PETINIA assay showed a systemic positive bias with a mean difference of $0.66 \mu\text{g/mL}$ (95% confidence interval [CI] $0.47-0.84 \mu\text{g/mL}$) compared with LC-MS. However, the magnitude of the positive bias decreased to $0.36 \mu\text{g/mL}$ (95% CI $0.29-0.44 \mu\text{g/mL}$) within the therapeutic range of MPA. Multiple logistic regression showed that MPA trough level determined by PETINIA assay was an independent risk factor for adverse event (hazard ratio 2.28, 95% CI 1.25-4.16, $p=0.007$). MPA trough level predicted adverse events with a sensitivity of 77.8% and a specificity of 86.7% using a cutoff level of $5.25 \mu\text{g/mL}$.

Conclusions: Positive bias of PETINIA over LC-MS assay was observed when measuring MPA concentration. However, correlation between two methods warrant that PETINIA assay is an acceptable method for the monitoring of the therapeutic MPA level. Furthermore, MPA trough level obtained by PETINIA is a useful monitoring tool to minimize toxicity in KTRs.

Key Words: Mycophenolate, Kidney transplantation, Trough level