Poster

[P25-6] P25-6: Immunosuppressive drugs (1): LC-MS/MS assay

Chair: Tsutomu Nakamura, Japan

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[P25-6-1] Comparison of PETINIA and LC-MS/MS for determining plasma mycophenolic acid concentrations in Japanese lung transplant recipients

Masafumi Kikuchi[1], Masaki Tanaka[2], Shinya Takasaki[3], Akiko Takahashi[4], Miki Akiba[5], Yasushi Matsuda[6], Masafumi Noda[7], Kanehiko Hisamichi[8], Hiroaki Yamaguchi[9], Yoshinori Okada[10], Nariyasu Mano[11] (1.Tohoku University Hospital, 2.Tohoku University Hospital, 3.Tohoku University Hospital, 4.Tohoku University Hospital, 5.Tohoku University Hospital, 6.Tohoku University Hospital, 7.Tohoku University Hospital, 8.Tohoku University Hospital, 9.Tohoku University Hospital, 10.Tohoku University Hospital, 11.Tohoku University Hospital)

Keywords: Mycophenolic acid, PETINIA, LC-MS/MS, Positive bias

Background

Mycophenolic acid (MPA) requires therapeutic drug monitoring to improve the outcome after organ transplantation. Recently, Siemens Healthcare Diagnostics developed a particle enhanced turbidimetric inhibition immunoassay (PETINIA) for determining plasma MPA. However, as the method shows cross-reactivity with the pharmacologically active acyl-MPA glucronide (AcMPAG), plasma MPA concentration is overestimated in liver, kidney, and heart transplant patients. The aim of this study was to compare MPA concentrations in plasma from lung transplant recipients by PETINIA with a reference liquid chromatography tandem mass spectrometry (LC-MS/MS).

Methods

Sixty blood samples were obtained, before, 0.5 h after, and 2 h after mycophenolate mofetil (MMF) administration, from 20 Japanese lung transplant patients (5 men and 15 women; median age 49 (23-65) years; MMF mean dose 787.5±373.1 mg/day). MMF was combined with tacrolimus and cyclosporine in 85% and 15% of patients, respectively. Blood samples were collected in 3 mL heparinized collection tubes, and centrifuged at 1,580 *g* for 10 min at 4 ˚C in order to obtain the plasma. We determined MPA concentration by PETINIA and LC-MS/MS on the same day.

Results

The mean MPA concentration measured by PETINIA was significantly higher than LC-MS/MS (3.26±2.73 mg/mL versus 2.82±2.71 mg/mL, $P<0.0001$). Although regression analysis showed strong linear relationship ($r^2 = 0.969$, $P<0.0001$) between PETINIA and LC-MS/MS, the result of the Passing Bablok analysis indicated a systematic difference with a slope of 1.104 (95% confidence interval [CI], 1.452-1.897) and an intercept of 0.229 (95%CI, 0.144-0.315). The Bland–Altman analysis reveals a mean bias of 0.44 mg/mL (95%CI, 0.32-0.56), comprising 26.25% (95%CI, 21.43-31.07). Plasma MPA concentration increased in accordance with sampling time (C0, C0.5, C2), but no change in absolute bias was observed. Thirty six measures (60%) fell out of the clinically acceptable range of 20%.

Conclusions

The measurement of MPA by PETINIA in lung transplant patients should evaluate the result with attention to

positive bias.