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Association of Mycophenolic Acid Trough Level with Adverse Events in Kidney Transplant Recipients

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Background: Mycophenolic acid (MPA) is a widely used immunosuppressant to prevent acute rejection in kidney transplant recipients (KTRs). However, therapeutic drug monitoring of MPA for predicting its toxicity have shown inconsistent efficacy. We investigated the correlation of MPA trough concentration (MPA C₀) with adverse events and transplant outcomes after kidney transplantation (KT).

Methods: This study included 82 patients who underwent KT. All KTRs received MPA with tacrolimus and steroid. MPA C₀ was determined monthly by using particle-enhanced turbidimetric inhibition immunoassay and clinical data were collected at each time point. Correlations between MPA dose and MPA C₀ were analyzed with Pearson's correlation. Clinical endpoints were biopsy-proven acute rejection (BPAR), leukopenia, anemia, thrombocytopenia, persistent diarrhea, and viral infection. To determine the effect of MPA C₀ on the clinical endpoints, we performed logistic regression analysis.

Results: MPA C₀ was not correlated with MPA dose during the study period ($r=0.112$, $p=0.354$). MPA C₀ was significantly higher in patients with leukopenia, anemia, thrombocytopenia and viral infection compared to patients without adverse events. (3.83 ± 1.41 mg/L vs. 2.69 ± 1.03 mg/L, $p<0.001$; 4.43 ± 1.28 mg/L vs. 2.76 ± 0.95 mg/L, $p<0.001$; 3.70 ± 1.21 mg/L vs. 2.83 ± 1.07 mg/L, $p=0.002$; 4.64 ± 2.26 mg/L vs. 2.80 ± 0.96 mg/L, $p=0.017$). Multiple logistic regression analysis revealed MPA C₀ was independent risk factor for each of the above adverse events. (odds ratio [OR] 2.28, 95% CI 1.44-3.59, $p<0.001$; OR 4.04, 95% CI 1.88-8.70, $p<0.001$; OR 2.22, 95% CI 1.29-3.81, $p=0.004$; OR 2.21, 95% CI 1.15-4.26, $p=0.018$). Receiver operated characteristic analysis showed that MPA C₀ of 3.54 mg/L, 3.79 mg/L, 3.53 mg/L and 4.27 mg/L were best predicted leukopenia, anemia, thrombocytopenia and viral infection, respectively. There was no association between MPA C₀ with BPAR in the observation periods.

Conclusion: MPA dose was not correlated with MPA C₀ in KTRs. High MPA C₀ increased the risk of leukopenia, anemia, thrombocytopenia and viral infection. Therefore, monitoring therapeutic trough level of MPA could be recommended to reduce MPA-related toxicity after KT.

Keywords: Kidney Transplantation, mycophenolic acid, toxicity, trough level