

Inosine monophosphate dehydrogenase activity depends on plasma concentrations of mycophenolic acid and its glucuronides in stable kidney transplant recipients

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Mycophenolic acid (MPA) belongs to the antimetabolite class of immunosuppressants used in organ transplant recipients for the prevention of acute rejection. Inosine monophosphate dehydrogenase (IMPDH) is a target of MPA, and its enzymatic activity has intra- and inter-patients variability. Although IMPDH activity has been considered as a pharmacodynamic indicator of MPA in kidney transplant recipients, factors affecting IMPDH activity remain to be clarified. The aim of this study was to evaluate the dependence of IMPDH activity on concentrations of MPA and its glucuronides (MPAG and AcMPAG) in kidney transplant recipients.

Seventy seven kidney transplant recipients (46 recipients were treated with mycophenolate mofetil [MMF] and 31 without MMF) in the stable medical condition were enrolled. Predose plasma concentrations (C_0) of MPA, MPAG, and AcMPAG and IMPDH activity in erythrocyte were determined using HPLC. IMPDH activity was compared between MMF-treated and non-MMF treated kidney transplant recipients. Stepwise multiple regression analysis was performed to assess the dependence between the IMPDH activity and 24 predictor values including MPA C_0 , MPAG C_0 , AcMPAG C_0 , and clinical laboratory values. The Ethics Committee of Hamamatsu University Hospital approved the protocol.

IMPDH activity was significantly higher in MMF-treated than non-MMF treated kidney transplant recipients ($P < 0.01$). In a multivariate analysis, AcMPAG C_0 , MPAG C_0 , and MPA C_0 , were important predictors explaining interindividual variability of IMPDH in stable kidney transplant recipients.

MMF treatment raised IMPDH activity in stable kidney transplant recipients. IMPDH activity may be a useful marker which reflects the long-term exposure of MPA and its glucuronides.