

# Pharmacokinetics and Pharmacodynamics of Mycophenolic Acid (MPA) in Diabetic Kidney Transplant Recipients

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**Purpose.** To evaluate the influence of diabetes on the pharmacokinetics (PK) and pharmacodynamics (PD) of MPA in 18 stable kidney transplant recipients. **Methods.** Diabetic patients (D, n=9) were matched with non diabetics (ND, n=9) based on demographic characteristics, time post transplant and renal function. All patients were on triple immunosuppressive regimen consisting of mycophenolate sodium, cyclosporine or tacrolimus and prednisone. After an overnight fast, a baseline blood sample (t=0) was obtained and patients were administered their daily dose of immunosuppressants followed by 12-hours blood sampling. Concentrations of total MPA and its phenol (MPAG) and acyl (AcMPAG) glucuronide metabolites as well as free MPA were measured in plasma by validated HPLC-UV and LC-MS/MS analytical methods, respectively. The activity of inosine 5'-monophosphate dehydrogenase (IMPDH) in lymphocytes, the molecular target of MPA was used as the PD marker and an indicator of cell based immune response to MPA. **Results.** No differences in PK parameters ( $C_{max}$ ,  $C_{min}$ ,  $T_{max}$  and  $AUC_{0-12}$ ) for total MPA, MPAG and AcMPAG or Free MPA were found between the two groups. In contrast the response to MPA was significantly higher in D patients despite comparable total and unbound concentrations of MPA. The geometric mean  $\pm$  std error of IMPDH activity ( $V_0$ ) ranged from  $10.54 \pm 1.41$  to  $18.86 \pm 1.52$  nmol XMP/hr/ $\mu$ g protein for D and  $28.34 \pm 1.30$  to  $51.29 \pm 1.55$  nmol XMP/hr/ $\mu$ g protein for ND (Figure). There were however no difference in IMPDH activity between controlled and uncontrolled diabetics. **Conclusions.** Diabetes does not alter the pharmacokinetics of MPA; however the IMPDH activity was significantly lower in diabetics and it was independent of the drug concentration or glycemic control.

