Influence of everolimus on mycophenolate mofetil pharmacokinetics in kidney transplant patients

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Background: The objective of this study was to assess the effect of everolimus (EVR) on the pharmacokinetic parameters of mycophenolate mofetil (MMF) in patients who underwent kidney transplantation (KTx).

Methods: Ten patients underwent KTx under triple immunosuppression which comprised of tacrolimus (Tac), MMF, and methylprednisolone (mPSL), and EVR was added at 3–6 months after KTx. The EVR dose was 1.5 mg/day and was adjusted to maintain the targeted trough blood concentration (C₀) of 3–8 ng/mL. At 4 weeks before and after the initiation of EVR, blood concentrations of Tac and MMF were measured before and 1, 2, 4, and 6 hours after administration, and the estimated value of the area under the concentration-time curve from 0 to 12 hours (AUC_{0–12}) was calculated. We compared the C₀ and AUC_{0–12} per dose of Tac and MMF before and after the initiation of EVR. We did not change the dose of Tac, MMF, and mPSL until 4 weeks after the initiation of EVR.

Results: The C₀ of EVR at 4 weeks after EVR addition was 5.1±1.3 ng/mL, which was within the targeted range in all patients. The mean estimated glomerular filtration rate at 4 weeks before and after the initiation of EVR was almost at the same level. The mean dose of Tac and dose per weight of MMF during the observation period were 7.2±4.2 mg/day and 19.0±6.5 mg/kg/day, respectively. The Tac C₀ per dose and the Tac AUC per dose before and after EVR addition were 1.16±0.57 and 1.18±0.68 ng/mL/mg and 46.3±18.0 and 48.1±22.9 ng·hr/mL/mg, respectively. The MMF C₀ per dose and the MMF AUC per dose before and after EVR addition were 19.0±0.63 and 22.0±1.3 ng/mL/g and 43.0±20.0 and 51.0±15.0 ng·hr/mL/g, respectively.

Conclusions: The EVR administration has no significant influence on the pharmacokinetics of MMF.

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