Tacrolimus Metabolism and Renal Function Following Renal Transplantation Using Once-Daily Envarsus XR as Compared to Twice-Daily Prograf

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BACKGROUND

Tacrolimus (Tac) is the most commonly used maintenance immunosuppressive calcineurin inhibitor (CNI) in renal transplantation. Tac metabolism is known to vary widely across transplant recipients, particularly among African Americans,1 and excess exposure to the drug may contribute significantly to CNI-nephrotoxicity over the long term. It has previously been shown that faster metabolism of Tac is associated with impaired renal function after transplantation, likely due to CNI-nephrotoxicity.2,3

OBJECTIVES

In this prospective randomized preliminary study, we sought to investigate the impact of Tac metabolism rate on nephrotoxicity after renal transplantation. We analyzed differences in Tac metabolism and renal outcomes in renal transplant patients receiving a once-daily extended release Tac formulation (Envarsus XR) or a twice-daily immediate release Tac formulation (Prograf). We hypothesized that patients treated with Envarsus XR may achieve more consistent calcineurin exposure with overall lower doses of Tac, decreasing the risk of CNI nephrotoxicity.

We also investigated differences in Tac metabolism and renal function outcomes among African American patients and patients of other races in the hopes of better predicting and avoiding CNI nephrotoxicity.

METHODS

• 50 renal transplant recipients were randomized to receive Envarsus XR or Prograf, 45 of whom were observed for one year following transplantation.

• Tacrolimus metabolism was assessed by calculating the ratio of the Tac blood trough concentration and the total daily Tac dose and was measured at least once every 30 days for 360 days.

• CNI-nephrotoxicity was assessed by serial collection of serum creatinine levels at least once every 30 days for 360 days.

RESULTS

• No significant differences were observed between Prograf and Envarsus XR groups with regards to Tac metabolism rate.

• African American recipients demonstrated faster Tac metabolism and higher mean serum creatinine levels than other study participants, suggesting higher risk for CNI-nephrotoxicity.

DISCUSSION

As the rate of Tac metabolism has previously been shown to impact renal function after transplantation, a sufficiently powered study will be needed to identify the potential benefits of Envarsus XR in reducing CNI nephrotoxicity, particularly in patients with high rates of Tac metabolism, such as African Americans.

REFERENCES


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