Tacrolimus metabolism and impact on graft function: A single center experience

Wong YH[1], Wong HS[1,2], Yakob S[1]

[1]Department of Nephrology, Hospital Selayang, [2]Clinical Research Center, Hospital Selayang

ABSTRACT

Introduction: Tacrolimus is part of standard immunosuppressive regimen after renal transplant. It has high inter-individual variable metabolism; genetic polymorphism has shown to significantly influence tacrolimus metabolism. Literature suggests that tacrolimus metabolism may have influence on renal graft outcome. This study aims to determine the impact of tacrolimus metabolism on graft function. **Materials and Methods:** This is a single centre, retrospective, observational cohort study from year 2000 to 2021. Data analysis was done using SPSS version 26. Tacrolimus metabolism rate was determined by concentration: dose (C/D) ratio at third month post transplantation. Patients with Tacrolimus C/D ratio < 1 ng/ml are characterized as fast metabolizers and ≥ 1 are characterized as slow metabolizers. Subjects' characteristic and eGFR were compared and analyzed. **Results:** In this study, 78 subjects were included and 9 were classified as fast metabolizers with a mean C/D ratio of 0.725. Age, genders, race, diabetes, hypertension status, induction agent and cold ischemic time were not associated with C/D ratio ($p > 0.05$). At 3 months post-transplantation, fast metabolizers comparing to slow metabolizers, had higher mean tacrolimus dose with 8.06 mg vs 3.82 mg ($p<0.001$) and demonstrated having lower mean trough levels 5.81ng/ml vs 8.23ng/ml ($p=0.016$) respectively. However, there is no statistical difference in graft function at 3, 6, 9, 12 and 24th month for both groups. **Conclusion:** In previous literatures, fast tacrolimus metabolizers are associated with worse graft outcome. In our study, there was no statistical difference in graft function observed between fast and slow metabolizers despite significant difference in dosage and trough levels of tacrolimus. The possible limitations include a small study population, short study duration as well as possible confounding factor of diltiazem usage.