

Predictors of Adverse Events and Determinants of the Voriconazole Trough Concentration in Kidney Transplantation Recipients Yan M, Zhao YC, Lin XB, Zhang BK

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Abstract

Background: Voriconazole (VRC) is the mainstay for the treatment of invasive fungal infections in kidney transplant patients, but it has many adverse events (AEs) and characteristics of variable pharmacokinetic. Aim of the article was to identify predictors of AEs using binary logistic regression and determinations of its trough concentration using multiple linear modeling.

Methods: From January 1, 2016 to December 31, 2019, hospitalization renal recipients were eligible to enroll in the study. The AEs were monitored throughout the study. All these statistics such as the demographic information, trough concentration, *CYP2C19* genotypes were all recorded by a standardized Case Report Form.

Results: We conducted a prospective analysis of 93 kidney recipients co-treated with VRC and collected 213 VRC trough concentration. Predictors of the AEs were VRC trough concentration (HR:2.614; $P=0.016$), *CYP2C19*-intermediate metabolizer (HR:0.009; $P=0.002$) and hemoglobin (HR:0.181; $P=0.005$). The predictive power of these three factors was 91.30%. Meanwhile, compared to patients carrying the *CYP2C19* poor metabolizer, trough concentration would decrease by 1.23($P < 0.001$) in intermediate metabolizer or by 1.521 ($P < 0.001$) in normal metabolizer respectively. Simultaneously, it would increase for the factor of hemoglobin by 0.021($P < 0.001$). Conversely, it would decrease because of a higher count of blood platelet($P=0.004$) and concomitant use of Ilaprazole($P=0.001$).

Conclusions: *CYP2C19* genotype and several other clinical variables were identified as perfect predictors of the AEs and biologically plausible modulators of the magnitude of VRC trough concentration, which could maximum the treat effect and minimize adverse events.

Keywords: Kidney transplantation recipients; voriconazole; adverse events; *CYP2C19* polymorphism; trough concentration.

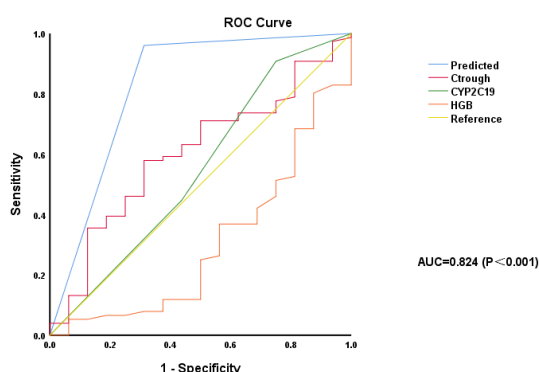


Figure.1: Receiver operating characteristic (ROC) curve for predicting adverse events.