# Population Pharmacokinetics of Voriconazole and C-reactive protein guided Dosage Optimization in Chinese Patients with Talaromyces marneffei Infection

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## Abstract

Objective To evaluate the population pharmacokinetics of voriconazole (VRC) and identify the factors affecting it in Chinese patients with Talaromyces marneffei infection. Based on the final model, the optimal dosing regimen was further investigated in these patients. Methods Patients with talaromycosis from two hospitals who met the inclusion criteria were enrolled. Patients' demographic information, VRC medication history, concomitant medications and laboratory test information data were recorded. A population pharmacokinetic model was developed through from the nonlinear mixed-effects models (NONMEM). Monte Carlo Simulation was applied to optimize the initial dosing regimens. Results A total of 146 blood samples taken from 46 patients with talaromycosis were included in the study. A one-compartment model was used to characterize VRC pharmacokinetics. Population estimates of clearance (CL) and volume of distribution (V) were 2.19 L/h and 88.4L, respectively. VRC clearance was significantly associated with C-reactive protein (CRP) level, which causing individual pharmacokinetics variation. CYP2C19 polymorphisms had no effect on voriconazole pharmacokinetic parameters. Based on the dosing simulations with CRP level, the initial dosing regimens was recommended are as follows: loading dose 150mg q12h 1day followed by maintenance dose 100mg q12h intravenous for CRP< 40mg/L, and loading dose 75mg q12h followed by maintenance dose 50mg q12h intravenous for CRP [?] 40mg/L. Conclusion A population pharmacokinetic model of VRC was successfully established in patients with Talaromyces marneffei infection. CRP was identified to significantly affect VRC plasma concentration. Optimizing initial dosing regimens according to the CRP level may be useful to guide VRC dosing in clinical practice.

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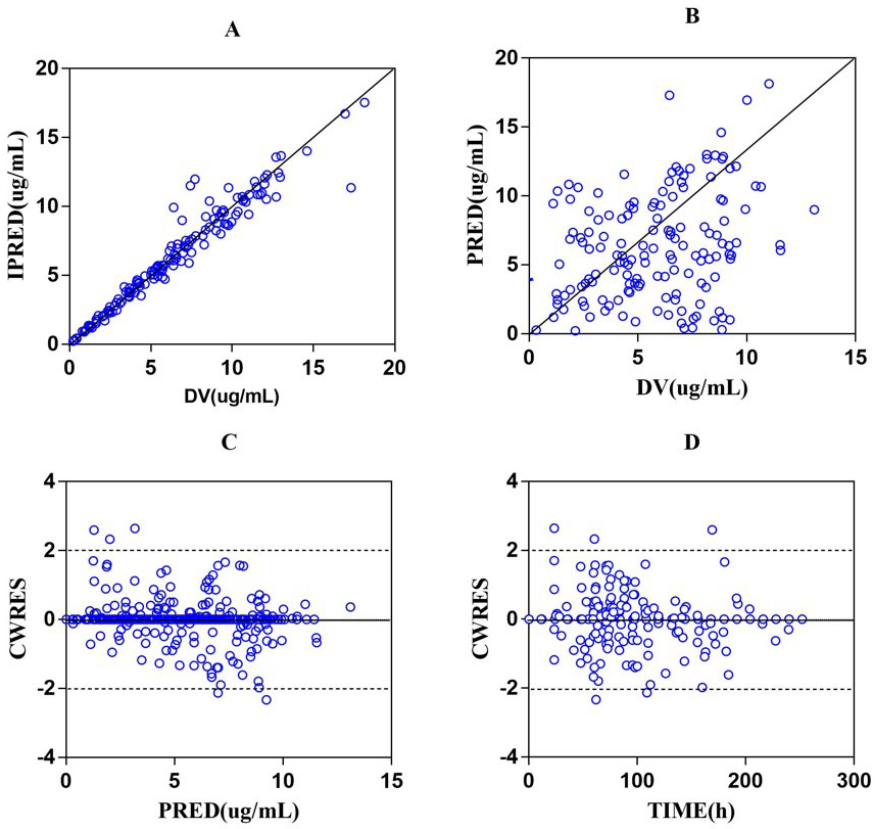


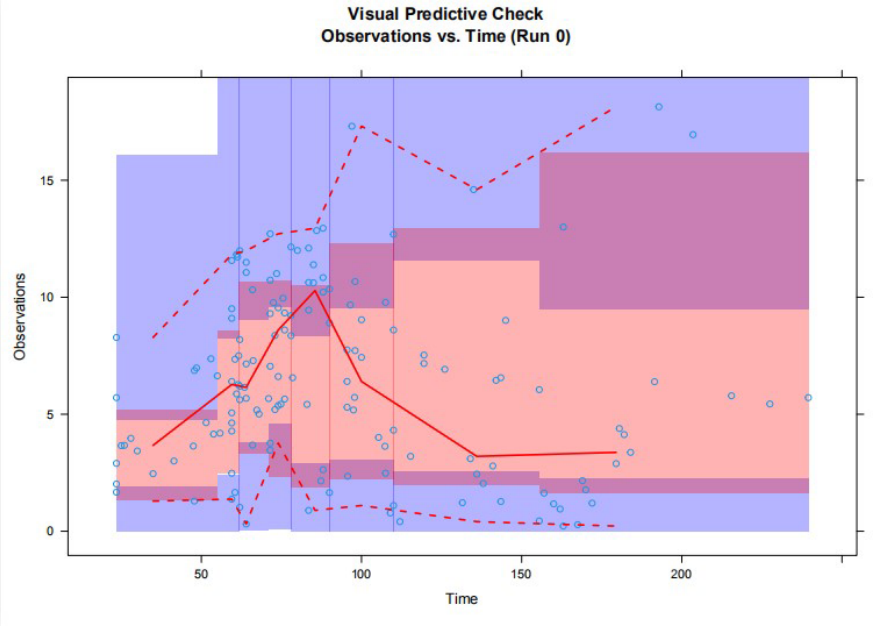

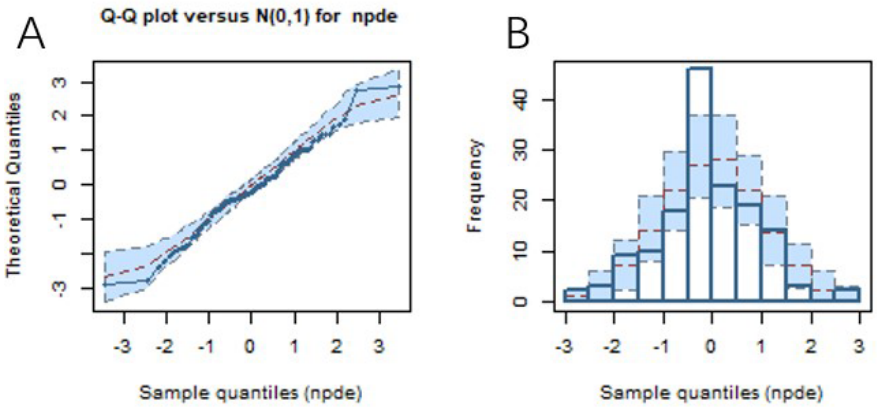


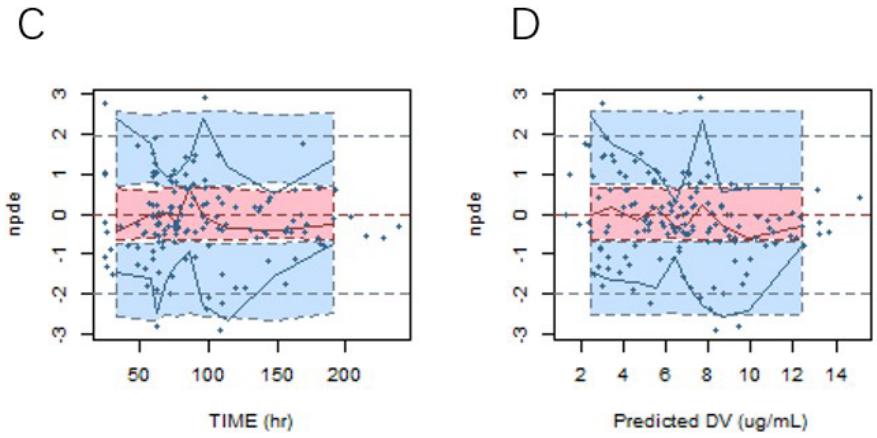


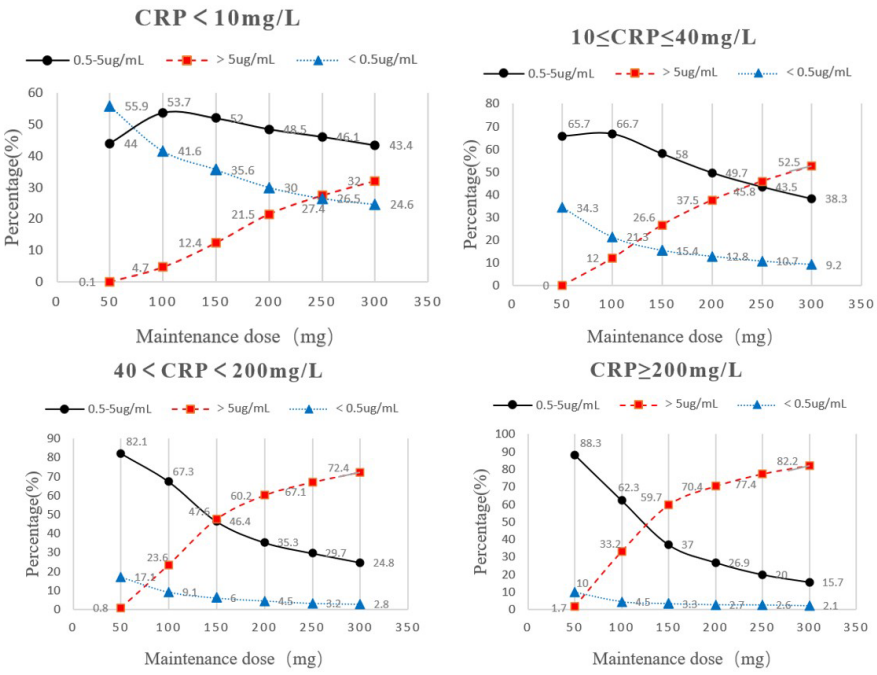

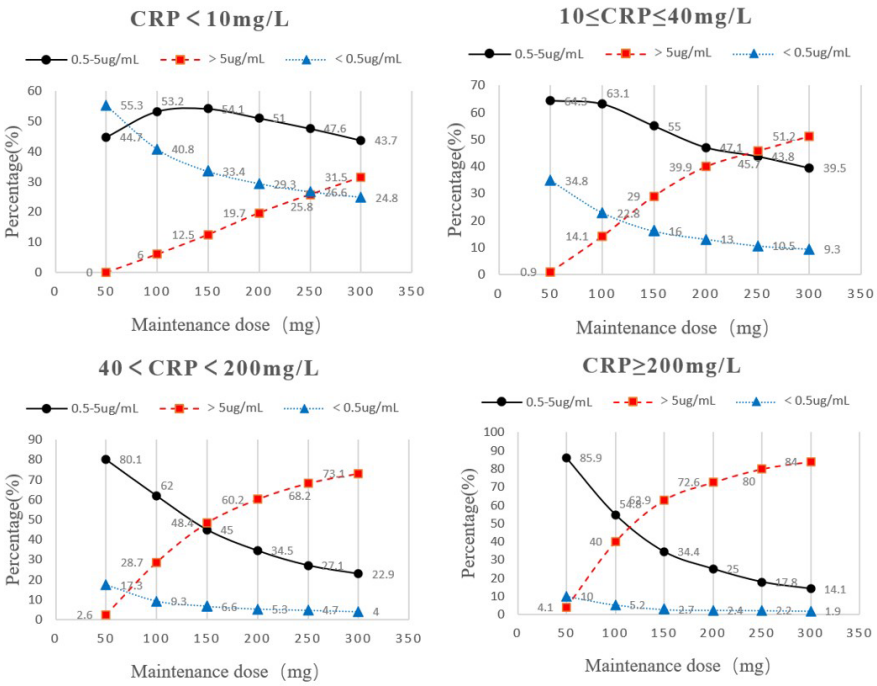


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