Therapeutic drug monitoring and safety evaluation of Voriconazole in the treatment of pulmonary fungal diseases

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Abstract

Aims: To investigate the relationship between steady-state voriconazole trough concentration (Ctrough) and adverse effects (AEs). Methods: We conducted a retrospective study in the Jinling Hospital from January 2015 to June 2020. A total of 140 patients receiving voriconazole were enrolled in this study. The determination and scoring of voriconazole-associated hepatotoxicity were performed according to the Roussel Uclaf Causality Assessment Method scoring scale and the severity of hepatotoxicity was graded according to CTCAE. Results: Compared to the group without any AEs, voriconazole Ctrough was significantly higher in the hepatotoxicity and neurotoxicity groups; however, no differences were observed in other AEs. Receiver operating characteristic (ROC) curves showed that steady-state voriconazole Ctrough >3.61 mg/L was associated with an increased incidence of hepatotoxicity (AUC=0.645, P=0.047). Logistic regression analysis showed that timely voriconazole dose adjustment was a predictor of attenuated hepatotoxicity after adjustment for confounders, but hepatotoxicity was not associated with voriconazole Ctrough measured at a single time point. When gamma-glutamyl transpeptidase (GGT) was included in the assessment of hepatotoxicity severity, its AE was overestimated. Steady-state voriconazole Ctrough and length of treatment were associated with GGT elevation. Conclusions: Despite an increasing trend of hepatotoxicity and neurotoxicity with increasing steady-state voriconazole Ctrough, it may not be sufficient for predicting the probability of hepatotoxicity. Concomitant co-monitoring of liver function parameters for 2 weeks after dosing may provide greater prevention of hepatotoxic events. In patients with long-term voriconazole usage, GGT is not a reliable indicator of hepatotoxicity, but it can be used to assess oxidative stress levels.

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