810. Voriconazole Dose Modification Guideline to Optimize Therapeutic Levels in Patients With Hematologic Malignancies
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Background. Voriconazole is an azole antifungal utilized for the prevention or treatment of systemic fungal infections in hematologic malignancies and hematopoietic stem cell transplantation (HSCT). Voriconazole has a non-linear pharmacokinetic profile with wide inter-patient variability, which makes dosing challenging. Previous studies have shown decreased efficacy and increased toxicity with subtherapeutic and supratherapeutic levels, respectively. Although therapeutic drug monitoring (TDM) of voriconazole is recommended, no established dosing guidelines have been elucidated. The objective of this retrospective study is to evaluate the dose modification strategies with voriconazole TDM and develop dosing guidelines to optimize therapeutic levels.

Methods. This study was a retrospective review of hospitalized patients with a history of hematological malignancies who received voriconazole between 1 June 2012 and 31 December 2013. Eligible adult patients (≥18 years of age) with a history of hematological malignancies initiating voriconazole for prophylaxis or treatment with at least two voriconazole trough levels reported were included. Age, gender, race, body mass index (BMI), proton pump inhibitor use, primary diagnosis, primary reason for admission, and indication for voriconazole were documented.

Results. Ninety-seven patients with 147 admissions were initiated on voriconazole during the study period. A total of 43 of 97 (44%) initial voriconazole trough levels were non-therapeutic (30 out of 97 (31%) were <1 mcg/mL and 13 out of 97 (13%) were >4 mcg/mL). The median initial steady state voriconazole trough level with standard 200 mg PO q12h with and without a loading dose was 2.8 mcg/mL and 1.8 mcg/mL, respectively (P = 0.34). Differences in baseline characteristics were not statistically significant after analysis using a χ² test in therapeutic versus non-therapeutic groups.

Conclusion. Standard dosing of voriconazole of 200 mg PO q12h may not be sufficient to achieve initial therapeutic trough levels in steady state. A pooled analysis of 125 dose modifications based on 531 levels was used to develop the voriconazole dose adjustment guideline in order to optimize achieving therapeutic levels in a timely fashion (table 1).

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