Optimized Administration of Voriconazole and Therapeutic Drug Monitoring in Children and Adolescents: A Single-Centre Retrospective Experience from China

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Abstract

Background: Voriconazole (VRC) is a triazole anti-fungal agent and a first-line treatment for invasive fungal infection (IFI) generally. There is an obvious variation in metabolism between children and adults. The purpose of this single-center retrospective study was performed to explore the factors affecting voriconazole trough concentration(C_{trough}) and to show VRC dose adjustment experience in children of several age groups in our centre.

Methods: The demographic information, concentration data, *CYP2C19* genotypes and clinical outcomes of eligible children from January 1th, 2016 to December 31th, 2018 were retrospectively collected. Factors affecting the voriconazole trough concentration were statistically analyzed.

Results: A total of 145 trough concentrations in 94 patients were included in this study. 62.8.%(59 in 94) of patients achieved one or more therapeutic level. In all blood samples, 54.5% of them achieved the target concentrations; however, 35.9% were sub-therapeutic and 9.6% were super-therapeutic post multiple VRC dosing. For children ≤2, 2-6, 6-12, and 12-18 years, the median VRC maintenance doses of 5.7, 6.7, 5.0 and 3.3 mg/kg twice daily respectively had been required in order to achieve therapeutic level (P<0.001), which were lower than major recommended doses and VRC package insert doses. Co-administration of proton pump inhibitors was also an important factor that significantly affected VRC target trough concentration (P=0.001). No correlation between the maintenance dose and *CYP2C19* genotypes along with the route of VRC administration was found due to small size of sampling.

Conclusions: In order to ensure the effectiveness and safety of voriconazole in children, early and repeat monitoring of voriconazole serum concentration is a powerful tool. Younger pediatric patients might need a higher dosage regime to achieve therapeutic trough concentration. The determination of voriconazole initial dose based on *CYP2C19* genotypes may also be a clinical decision-making method, which needs to be confirmed by further studies.

Keywords: Voriconazole, therapeutic drug monitoring, trough concentration, *CYP2C19*, genotype.