Pharmacogenetic Analysis of Voriconazole Treatment in Children.

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Voriconazole is among the first-line antifungal drugs to treat invasive fungal infections in children and known for its pronounced inter- and intraindividual pharmacokinetic variability. Polymorphisms in genes involved in the metabolism and transport of voriconazole are thought to influence serum concentrations and eventually the therapeutic outcome. To investigate the impact of these genetic variants and other covariates on voriconazole trough concentrations, we performed a retrospective data analysis, where we used medication data from 36 children suffering from invasive fungal infections treated with voriconazole. Data were extracted from clinical information systems with the new infrastructure; SwissPK; cdw; , and linear mixed effects modelling was performed using R. Samples from 23 children were available for DNA extraction, from which 12 selected polymorphism were genotyped by real-time PCR. 192 (49.1%) of 391 trough serum concentrations measured were outside the recommended range. Voriconazole trough concentrations were influenced by polymorphisms within the metabolizing enzymes CYP2C19 and CYP3A4, and within the drug transporters ABCC2 and ABCG2, as well as by the co-medications ciprofloxacin, levetiracetam, and propranolol. In order to prescribe an optimal drug dosage, pre-emptive pharmacogenetic testing and careful consideration of co-medications in addition to therapeutic drug monitoring might improve voriconazole treatment outcome of children with invasive fungal infections.

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