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ePoster Viewing
Evolving therapeutic strategies for fungal infections

A HIGH PERCENTAGE OF PATIENTS HAVE OFF-TARGET TROUGH VORICONAZOLE SERUM LEVELS

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Objectives: Voriconazole serum levels are unpredictable. Patients with low voriconazole levels (<1 µg/ml) show a poor clinical response, and patients with high levels (>5.5 µg/ml) are more likely to experience toxicity. Therapeutic drug monitoring (TDM) of voriconazole has been performed mostly in selected groups of patients; furthermore, very few studies report 'real-life' experience with TDM. We report data on TDM of voriconazole in serum samples from patients managed at different hospitals in Madrid during a three-year period (January 2011 to November 2013).

Methods: Clinical and demographic data were recorded. Samples were collected at the attending physician's discretion and stored at 4ºC from collection to processing. Trough serum voriconazole concentrations were measured using HPLC, as previously reported (Gordien and colleagues; J Pharm Biomed Anal. 2009). Serum voriconazole levels were considered sub-therapeutic (<1 µg/ml), on-target (1-5.5 µg/ml), or high (>5.5 µg/ml). The number of on-target levels found in the first sample and in the subsequent samples was studied and compared.

Results: We received 248 serum samples from 102 patients, most of whom were managed in 5 hospitals. Most patients were male (68%) and had the following underlying conditions: haematological cancer (43%), chronic obstructive pulmonary disease (14%), human immunodeficiency virus (9%), solid cancer (5%), and other. The clinical indication for voriconazole was mainly treatment of invasive aspergillosis (69%) and other forms of aspergillosis (7%), and prophylaxis (14%). Patients were managed in the following wards: haematology (37%), medical (32%), infectious diseases (11%), paediatrics (10%), and other (10%). The main reasons for TDM of voriconazole were initiation of antifungal treatment/prophylaxis (35%), patient monitoring (44%), and suspected toxicity (4%). Overall, voriconazole levels were sub-therapeutic in 18.5% of samples, on-target in 71.5%, and high in 10%. We did not find any association between reaching target serum voriconazole levels and the underlying condition (haematological diseases vs. other), the clinical indication for voriconazole (treatment vs. prophylaxis), or the route of administration (oral vs. intravenous). The proportion of samples with on-target levels was lower in the analysis of the first sample of each patient than in the subsequent samples studied (64% vs. 77%; $P<0.05$) (Figure).

Conclusion: We showed that a high proportion (28%) of voriconazole levels were off-target at initiation of antifungal therapy or prophylaxis. Samples collected under therapy administered for control purposes yielded a lower percentage of both sub-therapeutic and high voriconazole levels, suggesting that TDM of voriconazole was useful for optimization of antifungal therapy.