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Audit of voriconazole therapeutic drug monitoring in an English hospital after the implementation of electronic prescribing (EPIC)

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Background: Voriconazole is a triazole antifungal that is commonly used in the treatment of invasive aspergillosis. Therapeutic drug monitoring (TDM) is key to the effective use of voriconazole as the non-linear pharmacokinetics exhibited by the drug means conventional dosing often either fails to achieve satisfactory treatment outcomes or results in toxicity. Furthermore voriconazole serum concentrations are influenced by several factors including age, weight, genetic polymorphisms, altered drug absorption and drug interactions. Voriconazole trough levels greater than 6mg/L are associated with an increased likelihood of hepatotoxicity and the evidence to support the use of TDM during voriconazole treatment is growing. This audit investigated the TDM practices used during voriconazole treatment at Cambridge University Hospitals NHS Foundation Trust (CUH) between January-March 2016.

Material/methods: Data from all inpatients being treated with voriconazole was collected retrospectively over the three month period. Patients were identified using the Epic system and in-house dispensing reports. Voriconazole pre-dose serum levels were analysed by the Mycology Reference Laboratory, Bristol, England. Outpatient use of voriconazole was excluded, whilst patients who died before voriconazole levels were reported were removed from the study.

Results: 39 patients were identified as receiving voriconazole, of which 5 were deemed not suitable to receive TDM (i.e. long-term prophylaxis, short inpatient stay, etc.). A total of 22 voriconazole levels were reported for the remaining 34 patients. 8 of these patients actually commenced voriconazole treatment during the audit; all of which having their levels taken at an appropriate time (trough level, 5-7 days after treatment initiation).

In patients where a voriconazole level was taken, 68% were within therapeutic range (1-5.5mg/L). No levels were reported as potentially toxic (>6mg/L). Figure 1 summarises the distribution of

voriconazole levels reported. None of the voriconazole levels were reported back to CUH within the pre-stipulated 3 day turnaround window (mean turnaround time 10.7 days).

Pharmacist interventions that recommended voriconazole TDM should be instigated were recorded in 50% of cases. 100% of voriconazole prescriptions were either approved by microbiology or recommended as part of in-house guidelines.

Conclusions: This audit demonstrates that although TDM appears to be occurring at appropriate times for patients newly initiated on voriconazole, around one third of suitable patients are not having any voriconazole levels taken. Despite zero levels being reported within the toxic range, a significant proportion of levels were reported as sub-therapeutic (<1.5mg/L). This is worrying as the sub-optimal use of an expensive anti-infective agent introduces problems both in terms of antimicrobial resistance and wasted resources. This is compounded by the lack of in-house voriconazole assay facilities, which introduces a significant lag-time in the reporting of levels and therefore prevents the timely adjustment of doses where treatment falls outside of the therapeutic window.