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2112. Voriconazole for Primary Prophylaxis: A Decade of Trends and Outcomes

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Background. Invasive fungal infections (IFI) continue to affect the immunocompromised patient population. Many of these patients require antifungal prophylaxis. Voriconazole is an azole antifungal that has been utilized for preventing IFIs but does not have an approved indication for prophylaxis.

Methods. Adult patients admitted to Duke University Hospital from January 1, 2005 to December 31, 2015 who had received at least 2 days of systemic voriconazole as primary prophylaxis were included in this retrospective medical records review. Demographics, underlying comorbidities, adverse events, drug interactions, voriconazole blood concentrations, and microbiological data were assessed.

Results. Our review identified 403 patients receiving voriconazole for primary prophylaxis. 220 (55.6%) were male, 303 (75.2%) were Caucasian, and the mean age was 46.0 ± 15.7 years. 233 (57.8%) had leukemia, and 63 (15.6%) had lymphoma. 301 (74.7%) underwent hematopoietic transplant (BMT), and 45 (11.2%) had a solid-organ transplant. 176 (43.7%) patients received chemotherapy and 261 (64.8%) received immunosuppressive drugs. The mean voriconazole total daily maintenance dose was 416.1 ± 65.9 mg (5.5 ± 1.6 mg/kg/day). Patients received inpatient voriconazole for a mean of 19.5 ± 16.5 days. 371 (92.1%) patients received a concomitant interacting drug. Only 140 (43.7%) patients had therapeutic drug monitoring. The mean first voriconazole serum concentration was 1.8 ± 1.7 mg/L. 87 (21.6%) patients discontinued voriconazole prematurely; 41 (10.2% overall) of these patients had an adverse event requiring discontinuation. 5 had breakthrough fungal infections with microbiological data identifying a fungal species, which included *Rhizopus* spp. among others.

Conclusion. Voriconazole is frequently used for primary prophylaxis of IFIs and most commonly in BMT. It appears to be relatively well tolerated with some adverse side-effects (~10%) despite many potential drug-drug interactions and provides appropriate fungal coverage for many immunosuppressed patients. However, few patients had breakthrough fungal infections while receiving voriconazole. In a real-world setting, voriconazole can provide antifungal prevention in certain high-risk patients.

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2113. Evaluation of Empiric Antifungal Therapy in Critically Ill Patients with Liver Disease, Sepsis, and No Evidence of Active Fungal Infection

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Background. While candidemia is uncommon in the immunocompetent, critically ill population, it is associated with longer lengths of stay (LOS), higher cost, and higher mortality. In critically ill patients with liver disease and sepsis of unknown origin, antifungals (AF) are commonly used empirically. Recent studies suggest that this practice may not improve clinical outcomes but had little representation of patients with liver disease. This study aims to evaluate clinical outcomes of critically ill patients with liver disease, sepsis, and no evidence of active fungal infection who received empiric AF vs. those who did not.

Methods. This was a single-center, retrospective review of adults with liver disease and sepsis, identified by ICD-10 codes, who were discharged from the intensive care unit (ICU) between October 1, 2015 and December 31, 2018. Patients with neutropenia, marrow or organ transplant, HIV infection, systemic immunosuppressants, or fungal infection at sepsis onset were excluded. The primary outcome was inpatient mortality. Secondary outcomes included ICU LOS, total LOS, and development of fungal bloodstream infection (BSI) > 48 hours after sepsis onset. Fisher's exact and Wilcoxon rank-sum tests were used to compare baseline characteristics. Multivariable logistic regression models were used to compare outcomes. Model covariates were variables with P-values < 0.2 in univariate analysis.

Results. A total of 119 patients were included with 92 receiving empiric AF (micafungin or fluconazole) and 27 receiving no AF. Patients receiving empiric AF were more likely to have hepatic disease upon admission and less likely to have a bacterial infection. Both groups were similar in intubation and vasopressor requirements, febrile episodes, and Candida score. Unadjusted inpatient mortality for empiric vs. no AF was 70.4% vs. 70.7%. Unadjusted ICU LOS, total LOS, and development of a fungal BSI were 10 vs. 11 days, 19 vs. 19 days, and 63.0% vs. 2.2% ($P < 0.001$). In multivariable models, there was no difference in inpatient mortality between groups (OR 1.20, 95% CI 0.77–1.63).

Conclusion. In critically ill patients with liver disease, sepsis, and no evidence of active fungal infection, receipt of empiric antifungal therapy did not improve inpatient mortality, ICU LOS, or total LOS but did reduce fungal BSI.

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2114. Correlation Between Antifungal Consumption and the Distribution of *Candida* Species in a Hospital in Colombia

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Background. In recent years, a shift toward non albicans *Candida* infections has been described. An increase in the prescription of antifungals has been attributed as the cause of this change, but this issue has not been evaluated in Colombia.

Methods. The distribution of *Candida* spp. over an 11-year period 2007–2018 were extracted of the software WHONET 5.6. Antifungal drug consumption was measured as the number of defined daily doses (DDD)/100 patient-days over a 6-year period 2012–2018. Spearman's coefficient was performed to find a correlation between antifungal consumption and distribution of *Candida* species.

Results. A total of 811 non-duplicate isolates of *Candida* spp. were included. An increase in the frequency of isolates was observed in the period 2013–2016 (Figure 1). The highest number of isolates were collected from the intensive care unit (ICU) (35.6%) followed of medical ward (22%). Non albicans *Candida* predominated (58%) in the period evaluated. The shift toward non albicans *Candida* was presented in 2015 (Figure 2). A non-homologous distribution of albicans vs. non-albicans was noted between ICU and general ward ($P = 0.026$). 152 (18.7%) isolates were recovered from blood. *C. parapsilosis* was the most commonly species identified in the blood cultures of ICU in contrast to *C. albicans* in general ward (Figures 3 and 4).

Intravenous fluconazole was the main antifungal prescribed in ICU (mean 0.094 DDD/100 PD). Oral fluconazole was the principal antifungal prescribed in a medical-surgery ward (mean 0.021 DDD/100 PD) and oncology unit (mean 0.429DDD/100 PD). None of the correlations between antifungal consumption and recovery of non albicans species reached a statistical significance.

Conclusion. The shift toward non albicans *Candida* is possible even in the presence of a low consumption of antifungals. This finding suggests the possibility of other contributing factors such as cross transmission and microbiome alteration.

