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P2278 Survival of patients with *Candida albicans* bloodstream infection treated with fluconazole is determined by heteroresistance and time-to-treatment

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Background:

Candida strains with acquired or intrinsic resistance to azoles are an emerging problem, driving a sharp rise in the use of echinocandins. However, the majority of patients who die of candidemia are infected with azole-susceptible strains. Whether patients with azole-susceptible candidemia can be safely treated with fluconazole is unclear. We aimed to validate the clinical utility of fluconazole heteroresistance testing in this population.

Materials/methods:

We searched for patients with *Candida albicans* bloodstream infection who received primary monotherapy with fluconazole. Fluconazole MIC was determined using CLSI M27 broth microdilution methodology. Heteroresistance was quantified using a disc diffusion assay and image analysis, and expressed as the fraction of growth (FOG) of colonies within an inhibition zone corresponding to 20% growth reduction (FOG_{20}). Survival analysis was performed with covariates related to the host (age, comorbidity), illness (severity of sepsis) and antifungal treatment (PK/PD, MIC and FOG).

Results:

Forty-six patients with *C. albicans* bloodstream infection were studied. Thirteen patients (28%) died within 30 days of first positive blood culture. Twenty-seven patients were treated with fluconazole within 24 h of candidemia onset (early treatment group). Forty-three of 46 *C. albicans* isolates (93%) were susceptible to fluconazole. Median FOG_{20} was 0.48 (range, 0.095 to 0.76). FOG_{20} values were similar between non-survivors and survivors for the entire cohort (P=0.08), but higher among non-survivors in the early treatment group (0.63 ± 0.01 versus 0.48 ± 0.04, P=0.03). Severity of sepsis (Pitt and SOFA scores) and patient characteristics (age and Charlson score) were associated with mortality for the entire cohort, whereas fluconazole FOG_{20} >0.5 and dose/MIC <200 were significant predictors of mortality in the early treatment group (P=0.01 and P=0.03, respectively). For patients in the early treatment group, mortality was 50% versus 0% for FOG>0.5 and <0.5, respectively.

Conclusions:

Heteroresistance testing predicts the efficacy of fluconazole when started within 24 h of candidemia onset. Refinement of in vitro susceptibility testing to guide treatment of apparently susceptible *Candida* species may have implications for patient care and antifungal stewardship.