Fluconazole non-susceptible breakthrough candidemia after prolonged low-dose prophylaxis: a prospective FUNGINOS study


OBJECTIVES
Breakthrough candidemia (BTC) on fluconazole was associated with non-susceptible Candida spp. and increased mortality. This nationwide FUNGINOS study analyzed clinical and mycological BTC characteristics.

METHODS
3-year prospective study in 567 consecutive candidemias. Species identification and susceptibility testing (CLSI) in reference laboratory. Data analysis according to STROBE criteria.

RESULTS
43/576 (8%) BTC were studied: 37/43 (86%) on fluconazole (28 prophylaxis, median 200mg/day). 21% BTC vs. 23% non-BTC presented severe sepsis/septic shock. Overall mortality was 34% vs. 32%. BTC was associated with gastrointestinal mucositis (multivariate OR 5.25, 95%CI 2.23-12.40, p<0.001) and graft-versus-host-disease (6.25, 1.00-38.87, p=0.05), immunosuppression (2.42, 1.03-5.68, p=0.043), parenteral nutrition (2.87, 1.44-5.71, p=0.003). Non-albicans Candida were isolated in 58% BTC vs. 35% non-BTC (p=0.005). 63% of 16 BTC occurring after 10-day fluconazole were non-susceptible (Candida glabrata, Candida krusei, Candida norvegensis) vs. 19% of 21 BTC (C. glabrata) following shorter exposure (7.10, 1.60-31.30, p=0.007). Median fluconazole MIC was 4mg/l vs. 0.25mg/l (p<0.001). Ten-day fluconazole exposure predicted non-susceptible BTC with 73% accuracy.

CONCLUSIONS
Outcome of BTC and non-BTC was similar. Fluconazole non-susceptible BTC occurred in three out of four cases after prolonged low-dose prophylaxis. This implies reassessment of prophylaxis duration and rapid de-escalation of empirical therapy in BTC after short fluconazole exposure.
type

date of publishing

journal title

ISSN electronic

journal paper/review (English)

26-01-2018

J Infect

1532-2742