Wild-Type MIC Distributions and Epidemiological Cutoff Values for Selected Triazole and Echinocandin Antifungal Agents for Six Uncommon Species of Candida as Determined by CLSI Broth Microdilution Methods

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OBJECTIVES

- To describe the prevalence of isolates at ≤0.008 μg/mL caspofungin (CASP), ≤0.03 μg/mL fluconazole (FLC), and ≤0.015 μg/mL voriconazole (VOR) that were used to identify those isolates from the five most common Candida species (Candida albicans, C. glabrata, C. parapsilosis, C. tropicalis, and C. krusei) for triazole and echinocandin antifungal agents.
- To determine species-specific clinical breakpoints (CBPs) for triazole and echinocandin antifungal agents recently established species-specific clinical breakpoints (CBPs) for triazole and echinocandin antifungal agents.
- To determine whether the CBPs were validated.

METHODS

- Clinical isolates from 2001 to 2010 were collected from the SENTRY Antimicrobial Surveillance Program (SENTRY Program). To establish CBPs for each less common but yet more established antifungal agents. Thus, it is prudent to develop criteria, such as epidemiological cutoff values (ECVs), as a means of tracking the emergence of mechanisms (including or not) as a way to exhibit innate or acquired resistance to one or more established antifungal agents.

RESULTS

- The modal MIC distributions for anidulafungin, caspofungin, and the six species of Candida were determined species-specific ECVs for anidulafungin (ANF), caspofungin (CAS), and voriconazole (VRC) versus each of the six rare species of Candida.
- The ECVs were determined in a blinded manner by reclassifying the wild-type (WT) MIC distributions and considering the WT MIC distribution, the modal MIC for each WT isolate, and the inherent variability of the assay (usually ≤1 doubling dilution).

CONCLUSIONS

- These distributions show the overall favorable susceptibility profiles with C. parapsilosis and C. tropicalis, with wild-type echinocandin susceptibilities.
- The ECVs for caspofungin versus each of the six species of Candida were determined species-specific ECVs for each less common but yet more established antifungal agents. Thus, it is prudent to develop criteria, such as epidemiological cutoff values (ECVs), as a means of tracking the emergence of mechanisms (including or not) as a way to exhibit innate or acquired resistance to one or more established antifungal agents.

MATERIALS AND METHODS

Organisms: A list of 819 clinical isolates obtained from more than 50 medical centers worldwide from 2001 through 2010 were used in the study (SENTRY Program). The collection included 70 isolates of C. dubliniensis, 180 isolates of C. glabrata, 120 of C. parapsilosis, 70 of C. tropicalis, and 57 isolates of C. pelliculosa (Table 1). All isolates were obtained from blood or other normally sterile sites and represented the individual isolates from independent infectious episodes. The isolates were collected at individual study sites and were sent to the University of Iowa (Candida, and JMI Laboratories (SENTRY Program isolates, North Liberty, Iowa, USA) for identification and susceptibility testing. The isolates were also tested by standard methods supplemented by molecular identification techniques and stored as water suspensions until use in the study. Prior to testing, each isolate was streaked on blood agar base and incubated 24 hours.

RESULTS

The WT MIC distributions for anidulafungin, caspofungin, fluconazole, posaconazole, and voriconazole and each of the six species of Candida were determined species-specific ECVs for each less common but yet prevalent Candida species and antifungal agent.

- Among the echinocandins, the modal MIC values at 24 h of incubation ranged from 0.015 to 3 μg/mL for anidulafungin and 0.06 to 0.25 μg/mL for caspofungin, with higher values for VRC (Table 2).
- For the azoles, the modal MIC at 24 h of incubation ranged from 0.25 to 2 μg/mL for fluconazole, 0.03 to 0.12 μg/mL for posaconazole, and 1 to 12 μg/mL for voriconazole. The highest values were observed from C. parapsilosis (Table 2).
- Overall, C. dubliniensis and C. lusitaniae were the species displaying the lowest (≤0.008 μg/mL) anidulafungin and voriconazole susceptibility and azole activity (≥0.25 μg/mL for fluconazole). In general, the ECVs should encompass at least 50% of isolates in the WT distribution. Organisms with acquired or mutation resistance mechanisms may be included among those for which the MIC results are higher than the ECV.

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REFERENCES


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