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Monitoring Echinocandin and Azole Susceptibility in a Global Collection of Invasive Fungal Isolates

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Amended Abstract

Background: Continuous monitoring of antifungal susceptibility patterns and understanding resistance mechanisms are necessary to prevent and respond to potential outbreaks of antifungal resistance. The aim of this project was to describe the antifungal susceptibility patterns and resistance mechanisms among C. neoformans and other Candida species.

Materials and Methods: Fungal isolates collected during 2014-2015 in 29 countries were susceptible to three echinocandin microdilution methods. CLSI interpretive criteria and epidemiological cutoff values (ECVs) were determined for the echinocandins. Cmins isolates displaying echinocandin MICs were sequenced for the fks (1) and fks2 (2) genes. The expression of Erg11, CDR1, CDR2, and MDRI was determined by quantitative real-time PCR (RT-PCR) using high-throughput cDNA microarrays. Relative expression results were performed in triplicate to normalize to an endogenous reference genes (ERG11).

Results: Susceptibility rates for the most common CANS are displayed in Table 1. Three isolates (0.3%) had non-wild-type MIC results for fks1. Susceptibility rates for echinocandin MICs were 88.7% for anidulafungin, 100.0% for caspofungin, and 100.0% for micafungin (n=79). MICs for C. tropicalis were 8, 0.12, and 0.25 mg/L, respectively.

Conclusions: Monitoring of antifungal susceptibility patterns and understanding resistance mechanisms among C. neoformans and other Candida species are necessary to prevent and respond to potential outbreaks of antifungal resistance. The expression of Erg11, CDR1, CDR2, and MDRI was determined by quantitative real-time PCR (RT-PCR) using high-throughput cDNA microarrays. Relative expression results were performed in triplicate to normalize to an endogenous reference genes (ERG11).

Appendix: Table 1

<table>
<thead>
<tr>
<th>Antifungal agent</th>
<th>C. neoformans</th>
<th>C. krusei</th>
<th>C. glabrata</th>
<th>C. albicans ATCC 90028</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anidulafungin</td>
<td>88.7%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Micafungin</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Introduction

Invasive fungal infections (IFI) are associated with high mortality and mortality rates and elevated hospital care costs. Monitoring antifungal susceptibility patterns and resistance mechanisms to clinically used antifungal agents is important.

Materials and Methods

A total of 3,557 fungal consecutive non-ophthalmic isolates were collected from 68 hospitals in 29 countries (n=79). Microdilution methods were used for antifungal susceptibility testing. Cmins isolates displaying MICs were sequenced for the fks (1) and fks2 (2) genes. The expression of Erg11, CDR1, CDR2, and MDRI was determined by quantitative real-time PCR (RT-PCR) using high-throughput cDNA microarrays. Relative expression results were performed in triplicate to normalize to an endogenous reference genes (ERG11).

Results

• Resistance to the fluconazole was observed among 0.1% of C. albicans, 2.7% of C. tropicalis, and 5.6% of C. glabrata isolates.
• Voriconazole resistance was observed among 0.1% of C. albicans, 0.7% of C. tropicalis, and 2.8% of C. glabrata isolates.

Materials and Methods

A total of 3,557 fungal consecutive non-ophthalmic isolates were collected from 68 hospitals in 29 countries (n=79). Microdilution methods were used for antifungal susceptibility testing. Cmins isolates displaying MICs were sequenced for the fks (1) and fks2 (2) genes. The expression of Erg11, CDR1, CDR2, and MDRI was determined by quantitative real-time PCR (RT-PCR) using high-throughput cDNA microarrays. Relative expression results were performed in triplicate to normalize to an endogenous reference genes (ERG11).