Mutant prevention concentrations (MPCs) of micafungin and anidulafungin against Candida glabrata clinical isolates

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The mutant prevention concentration (MPC) is a parameter previously used to optimize antibacterial treatments minimizing the emergence of resistant isolates.

We assessed the MPCs and the mutant selection window (MSW) of anidulafungin and micafungin against C. glabrata isolates with the corresponding mutation frequency.

BACKGROUND and OBJECTIVE

METHODS

20 C. glabrata echinocandin-susceptible isolates

3-7x10⁹ CFU/mL

Streaked onto plates with micafungin/anidulafungin (0.015 to 2 mg/L)

Incubated up to 5 days

EUCAST MICs against the colonies growing onto plates containing 1 mg/L of micafungin or anidulafungin.

Sequence of fks1 and fks2 genes

MPC: Lowest echinocandin concentration on the agar plates leading to complete inhibition of fungal growth.

MSW: Range of concentrations between MIC and MPC.

Mutation frequency: Ratio between the number of fks mutant colonies growing onto plates containing 1 mg/L of micafungin/anidulafungin and the number of cells streaked.

RESULTS

The percentage of isolates growing on plates after 5 days of incubation is shown in the Table:

<table>
<thead>
<tr>
<th>Echinocandin concentrations (mg/L)</th>
<th>0.015</th>
<th>0.031</th>
<th>0.062</th>
<th>0.125</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anidulafungin (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>95</td>
<td>70</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>Micafungin (%)</td>
<td>100</td>
<td>100</td>
<td>85</td>
<td>80</td>
<td>55</td>
<td>35</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Both echinocandins showed similar MPC ranges. The micafungin MSW was narrower than the anidulafungin MSW. Mutation frequency was lower in the presence of micafungin compared to anidulafungin (P=0.02) (Figure 1):

A total of 12/20 isolates grew onto 1 mg/L micafungin/anidulafungin plates yielding 32 colonies phenotypically resistant as per EUCAST (Figure 2):

MPC range (GM): 0.125-2 mg/L

MSW (GM): 0.015-0.73 mg/L

M. frequency: 5.3-2.2 x10⁻⁸

MPC range (GM): 0.25-2 mg/L

MSW (GM): 0.025-1.15 mg/L

M. frequency: 3.9-1.7 x10⁻⁸

Table. Isolates growing on plates containing different concentration of micafungin and anidulafungin

CONCLUSIONS

Our study suggests that, overall, concentrations of anidulafungin and micafungin above ≥ 2 mg/L may prevent the emergence of C. glabrata fks2 mutant isolates.

In contrast, concentrations below 2 mg/L may promote the development of secondary resistance to echinocandins.

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