Review: Antifungal agents do not reduce mortality in neutropenia caused by chemotherapy or bone marrow transplantation


Question
In patients with cancer and neutropenia caused by chemotherapy or bone marrow transplantation (BMT), do antifungal agents reduce mortality?

Data Sources
Studies were identified by searching 2 electronic databases, conference abstracts, and bibliographies and by contacting pharmaceutical manufacturers.

Study Selection
Studies were selected if they were randomized controlled trials (RCTs) comparing antifungal agents with placebo or no treatment in patients with cancer and neutropenia caused by chemotherapy or BMT.

Data Extraction
Data were extracted on patients, intervention, treatment duration, length of follow-up, randomization, blinding, and outcomes (deaths, invasive fungal infections [IFIs], colonization, and use of rescue drugs).

Main Results
30 RCTs (4094 patients) were included. Patients had leukemia in 19 RCTs and BMT in 11 RCTs. Antifungal agents were used prophylactically in 27 RCTs and empirically in 3 RCTs. Treatment groups did not differ for mortality overall (Table) or when grouped by type of antifungal agent. Antifungal agents led to fewer infections overall; the treatment effect was seen for amphotericin, fluconazole, and itraconazole but not for ketoconazole or miconazole (Table).

Studies on colonization rates and use of rescue drugs were heterogeneous; antifungal agents led to lower rates of colonization and use of rescue drugs than did placebo or no treatment (Table).

Conclusions
In patients with cancer and neutropenia caused by chemotherapy or bone marrow transplantation, antifungal agents do not reduce mortality. Amphotericin, fluconazole, and itraconazole reduce invasive infection. Colonization and use of rescue drugs are reduced by antifungal agents.

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Antifungal agents vs placebo or no treatment for cancer with neutropenia*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Antifungal agent</th>
<th>Number of trials</th>
<th>Antifungal agents</th>
<th>Control</th>
<th>RR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>24</td>
<td>14.7%</td>
<td>15.4%</td>
<td>5% (−11 to 18)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Invasive infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>26</td>
<td>4.2%</td>
<td>8.6%</td>
<td>50% (36 to 61)</td>
<td>23 (17 to 35)</td>
</tr>
<tr>
<td></td>
<td>Amphotericin</td>
<td>7</td>
<td>2.7%</td>
<td>7.5%</td>
<td>61% (24 to 80)</td>
<td>21 (13 to 63)</td>
</tr>
<tr>
<td></td>
<td>Fluconazole</td>
<td>8</td>
<td>4.3%</td>
<td>11%</td>
<td>61% (43 to 73)</td>
<td>15 (11 to 24)</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>3</td>
<td>3.6%</td>
<td>7.2%</td>
<td>49% (4 to 73)</td>
<td>28 (15 to 334)</td>
</tr>
<tr>
<td></td>
<td>Miconazole</td>
<td>2</td>
<td>5.3%</td>
<td>10%</td>
<td>48% (−31 to 80)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

**Table:** *Abbreviations defined in Glossary; RR, RRR, NNT, NNH, and CI calculated from data in article using a fixed-effects model. Length of follow-up not reported.†Statistically significant heterogeneity existed among trials; random-effects model was used.

References