In vitro Susceptibilities of Candida Isolates From Patients with Endophthalmitis: Evaluation of Novel and Traditional Antifungal Agents

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Disclosures

• No financial disclosures
My role in this research

✓ Conception and design of the work/project
✓ Acquisition of data
✓ Analysis and interpretation of data
✓ Creation and/or critical review of the presentation
Introduction

- Fungal endophthalmitis can be associated with long treatment courses and poor outcomes
- Newer antifungal agents are currently available but limited data is published on their effectiveness
Introduction

Before 2000

After 2000
Introduction

Some newer, more expensive therapies have not been compared to more traditional drugs.

- **Posaconazole**
  - $4,096.57
  - 60 tabs

- **Anidulafungin**
  - $195.98
  - 100 mg vial

- **Voriconazole**
  - $163.82
  - 200 mg vial
Design & Methods

• Retrospective review of all patients with positive vitreous cultures of Candida species

• January 1, 2011 to September 30, 2017
Design & Methods

- Frozen samples were inoculated with 10,000 CFU/mL of yeast broth at a temperature of 35° C for 48 hours.

- Antifungal sensitivities to *Candida* were obtained for the following:

<table>
<thead>
<tr>
<th>Echinocandins</th>
<th>Caspofungin</th>
<th>Anidulafungin</th>
<th>Micafungin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triazoles</td>
<td>Voriconazole</td>
<td>Posaconazole</td>
<td>Itraconazole</td>
</tr>
<tr>
<td>Polyenes</td>
<td></td>
<td></td>
<td>Amphotericin B</td>
</tr>
<tr>
<td>Nucleoside Analogs</td>
<td></td>
<td></td>
<td>5-Flucytosine</td>
</tr>
</tbody>
</table>
Design & Methods

ETEST Strips

Sensititre YeastOne microdilution plates
Results

17 *Candida* isolates were identified:
- *C. albicans*: 10
- *C. glabrata*: 3
- *C. parapsilosis*: 2
- *C. tropicalis*: 2
## Results

<table>
<thead>
<tr>
<th>Drugs Used</th>
<th>Resistant Isolates (%)</th>
<th>MIC90 (ug/mL)</th>
<th>Resistant Isolates (%)</th>
<th>MIC90 (ug/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ETEST Strips</td>
<td>Microdilution Plates</td>
</tr>
<tr>
<td><strong>Echinocandins</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Caspofungin</td>
<td>0</td>
<td>0.03</td>
<td>0</td>
<td>0.11</td>
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<tr>
<td>Anidulafungin</td>
<td>--</td>
<td>--</td>
<td>15</td>
<td>0.42</td>
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<tr>
<td>Micafungin</td>
<td>--</td>
<td>--</td>
<td>0</td>
<td>0.05</td>
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<tr>
<td><strong>Triazoles</strong></td>
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<td></td>
</tr>
<tr>
<td>Voriconazole</td>
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<td>0.06</td>
<td>0</td>
<td>0.03</td>
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<tr>
<td>Posaconazole</td>
<td>0</td>
<td>0.79</td>
<td>0</td>
<td>0.12</td>
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<tr>
<td>Itraconazole</td>
<td>0</td>
<td>0.08</td>
<td>0</td>
<td>0.12</td>
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<tr>
<td>Fluconazole</td>
<td><strong>11.8</strong></td>
<td><strong>103</strong></td>
<td>0</td>
<td>1.00</td>
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<tr>
<td><strong>Polyenes</strong></td>
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<tr>
<td>Amphotericin B</td>
<td>0</td>
<td>0.12</td>
<td>0</td>
<td>0.50</td>
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<tr>
<td><strong>N. Analog</strong></td>
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<tr>
<td>5-Flucytosine</td>
<td>--</td>
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<td>0.06</td>
</tr>
</tbody>
</table>
Drug Efficacy (Time-to-Kill)

Fluconazole

Amphotericin

Posaconazole

Voriconazole
Is traditional better?

• Amphotericin B is efficacious but can be toxic to retinal ganglion cells at even levels as low as 5μg (Tremblay et al.)

• Second line agents are often necessary clinically

On histology: “Atrophy and focal necrosis of the retina ... hypertrophy of the RPE”

Reduced Toxicity of Liposome-Associated Amphotericin B Injected Intravitreally in Rabbits
Claude Tremblay,*† Michael Barza,*‡ Francis Szoka,§‡ Moshe Lahov,¶‖ and Jules Baum†‖

Comparison Within Drug Classes

What about the other agents?

**Comparison of Triazole MIC90 Values**
- Voriconazole MIC90 lower than other triazoles

**Comparison of Echinocandin MIC90 Values**
- Anidulafungin MIC90 higher than other echinocandins
Comparison Within Drug Classes

- Voriconazole has shown lower ocular toxicity, better penetration, and good clinical outcomes
- Growing body of case reports demonstrating clinical efficacy
Comparison Within Drug Classes

Comparison of Echinocandin MIC90 Values

- 1 rabbit model case series of 24 eyes vs. Voriconazole and Amphotericin B
- Clinically more effective (p < 0.05)
- Retinal toxicity lower than other groups (p < 0.05)

- 2 successful case reports of intravitreal caspofungin
- Safety studies demonstrating no evidence of toxicity on ERG vs. NaCl

- No intravitreal cases or studies have been reported

Summary of Findings

• Both newer and traditional antifungal agents are generally effective
• Mild Candida resistance was seen with fluconazole (older) and anidulafungin (newer)
• Newer therapies are not necessarily more efficacious than traditional!
Summary of Findings

• In-class agents:
  – *Voriconazole* showed ↓ MIC than fluconazole, itraconazole, posaconazole
  – *Micafungin* showed ↓ MIC than caspofungin, anidulafungin

• Further studies investigating these newer antifungals are necessary
Special Thanks to Bascom Palmer Eye Institute Microbiology
References


