(luconazole) or not?

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Objectives

- Discuss the need for antifungal stewardship
- Review the pharmacology of fluconazole
- Review *Candida sp.* susceptibility rates for fluconazole
- Review treatment guidelines (for adults)
- Discuss common fluconazole-stewardship opportunities in the hospital
Background

• My personal experience as an antimicrobial stewardship pharmacist is that antifungal agents are one of the most overprescribed antimicrobial classes in the inpatient setting.

• And antifungal agents are often overlooked when it comes to antimicrobial stewardship.
  • Particularly topical agents and fluconazole.
Fluconazole

• Triazole antifungal
  • Inhibits the development of ergosterol
  • Fungistatic

• Approved in the early 1990s and completely revolutionized the treatment of invasive fungal infections

• Compared to other azoles
  • Significantly fewer drug interactions
  • Only azole reliable for treatment of UTI
  • Well tolerated

Dose
150 to 1200 mg IV/PO daily
CrCl 10-50 mL/min: 50% of dose

Pharmacokinetics
Absorption: > 90%
Distribution: CSF, eye, bone, etc.
Metabolism/elimination: 30 hour half life, renal
### Spectrum of Activity

<table>
<thead>
<tr>
<th>Great Activity</th>
<th>Variable Activity</th>
<th>Poor Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Candida albicans</em></td>
<td><em>Candida glabrata</em></td>
<td><em>Candida krusei</em></td>
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<tr>
<td><em>Candida parapsilosis</em></td>
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<tr>
<td><em>Candida tropicalis</em></td>
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<tr>
<td><em>Cryptococcus neoformans</em></td>
<td></td>
<td><em>Aspergillus fumigatus</em></td>
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<tr>
<td>(step-down therapy)</td>
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<tr>
<td><em>Coccidioides immitis</em></td>
<td></td>
<td><em>Zygomycetes</em></td>
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</tbody>
</table>
### Local Inpatient Susceptibility Rates

<table>
<thead>
<tr>
<th>Yeast</th>
<th>Percent Susceptible to Fluconazole</th>
<th>Percent Susceptible Dose Dependent*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Candida albicans</em></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><em>Candida glabrata</em></td>
<td>Not applicable</td>
<td>≥50 %</td>
</tr>
</tbody>
</table>

*Needs doses of 400 to 800 mg or &gt; 6 mg/kg/day

- Echinocandin resistance has also occurred
Amphoterrible is a monster. He treats monster infections such as histoplasmosis and other life threatening fungal infections. He has a terrible habit of creating irregularities in the heart (arrhythmias). The X marks the spot of the kidney since 80% of clients receiving this drug may develop some nephrotoxicity.
Is Vitamin F Indicated?

References:
Asymptomatic Candiduria

“Treatment with antifungal agents is NOT recommended...almost always represents colonization..”

Exceptions: neutropenia, very low-birth-weight infants (< 1500 g), and patients who will undergo a urologic manipulation

Additional recommendations:
• Remove/replace indwelling catheter if feasible
Symptomatic *Candida* Cystitis

Fluconazole susceptible isolates: Fluconazole 200 mg (3 mg/kg) PO daily x 2 weeks

Additional recommendations:
- Remove/replace indwelling catheter if feasible
- Can be used for treatment of many resistant *Candida* isolates
  - Achieves urine concentrations 16 times higher than serum concentration

Commentary:
- Other potential causes of symptoms and should be pursued
Candida in the Urine

• Key points

• “…pyuria, in a patient with an indwelling bladder catheter cannot differentiate Candida infection from colonization.”

• “…the colony count in the urine, especially when a catheter is present, cannot be used to define infection.”
Candida in the Respiratory Tract

“Growth of Candida from respiratory secretions usually indicates colonization and rarely requires treatment with antifungal therapy.”

Exception:

• Systemic candidiasis: consider when patient is febrile, not responding to antibiotics, and yeast found in 2 or more places (i.e. skin, urine, lung, etc.)

Commentary:

• In general, northern Nevada does not care for patients at risk for Candida pneumonia; therefore, an ID consult is highly recommended if treatment is pursued
Candida in the Respiratory Tract

• Key points
  • “This almost always reflects colonization of the airway and not infection.”
  • Pneumonia generally only occurs in severely immunocompromised patients following hematogenous spread to the lungs.
  • “…a firm diagnosis requires histopathological evidence of invasive disease.”
  
• “Because of the rarity of Candida pneumonia, the extremely common finding of Candida in respiratory secretions, and the lack of specificity of this finding, a decision to initiate antifungal therapy should not be made on the basis of respiratory tract cultures alone.”
Oropharyngeal Candidiasis (not esophageal)

Mild disease:
Preferred: Clotrimazole troches 10 mg 5 times a day x 7-14 days OR
Alternative: Nystatin suspension 4-6 mL 4 times a day x 7-14 days

Moderate to severe or intubated:
Fluconazole 100-200 mg PO daily x 7 days
Vulvovaginal Candidiasis

Mild/uncomplicated disease:
Preferred: Any topical antifungal agent
Miconazole 200 mg suppository qHS x 3 days
Miconazole 100 mg suppository qHS x 7 days
Alternative: Fluconazole 150 mg PO x 1

Severe:
Fluconazole 150 mg PO q72h x 2-3 doses

Recurrent and on prolonged antibiotic therapy:
Fluconazole 100-200 mg PO daily x 10 to 14 days then 150 mg weekly
Candida Intertrigo

Mild/uncomplicated disease:
Any topical antifungal agent

Severe/refractory:
Fluconazole 100-200 mg daily x 7 days

Key Points

• Intertrigo is most commonly non-infectious
  • Drying agents, barrier agents preferred
• Erythema may remain even after successful treatment
Intra-abdominal Infections

“Empiric antifungal therapy for Candida is not recommended for adult and pediatric patients with community-acquired intra-abdominal infection”

“Empiric antifungal therapy should be considered for patients with clinical evidence of intra-abdominal infection and significant risk factors for candidiasis, including recent abdominal surgery, anastomotic leaks, or necrotizing pancreatitis”

If antifungal therapy is indicated:
Fluconazole 800 mg x 1 then 400 mg daily or echinocandin depending on risk for resistance and severity of disease
Summary of Treatment Guidelines

• Antifungals, including fluconazole, are not vitamins that should be given to everyone

• Fluconazole is NOT indicated for the following:
  • Asymptomatic candiduria (except neonates, neutropenia, and urological procedure)
  • *Candida* isolated solely from the respiratory tract
  • Mild oropharyngeal candidiasis
  • Uncomplicated *Candida* intertrigo
  • Empiric treatment of community-acquired intra-abdominal infections

• Fluconazole is not first line for vulvovaginal candidiasis
Role of the Antimicrobial Steward

- Assist the provider with the following
  - Determining whether or not antifungal treatment is indicated
  - If indicated, antifungal selection
  - Ensure appropriate dose, route, and duration
    - Get stop dates up front!!
- Don’t ignore topical anti-fungal therapy

Every Day, Every Dose
Antimicrobial Stewardship
Renown HEALTH