Azole-Resistant Vulvovaginal Candidiasis

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The presenter has no actual or potential conflicts of interest in relation to this presentation
Objectives

• Classify vulvovaginal candidiasis (VVC) in terms of severity

• Describe current treatment options for complicated and uncomplicated VVC

• Compare and contrast treatment options for azole-resistant *C. albicans* VVC
Patient Case

• **CC:** AD is a 33 YOF presenting to clinic with complaints of vaginal itching, soreness, and painful urination

• **HPI:** Positive for symptoms over the past 2-3 days; has had similar symptoms 3 times this year and was treated with fluconazole

• **Diagnosis:** Recurrent VVC

• **Culture Results:**

<table>
<thead>
<tr>
<th>Species</th>
<th>C. albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptibilities</td>
<td>Azole-resistant</td>
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Vulvovaginal Candidiasis Background

- Mucocutaneous infection
- Symptoms:
  - Pruritis, vaginal soreness, dysuria, dyspareunia, and changes in vaginal discharge

*C. albicans* isolated > 90%

Vulvovaginal Candidiasis Background

- Increasing prevalence over 10 years

- Causes
  - Empiric treatment
  - OTC over-utilization
  - Long duration, low-dose suppressive fluconazole therapy

C. albicans isolated > 90%

Azole-resistance 5-15%
Vulvovaginal Candidiasis Background

- **C. albicans isolated > 90%**
- **Azole-resistance 5-15%**
- **Recurrent VVC 5-8%**

- 90% cure rate after 6 months of treatment

VVC Severity Classification

- **Uncomplicated**
  - Infrequent episodes
  - Mild-to-moderate symptoms
  - Likely *C. albicans*

- **Complicated**
  - Recurrent
  - Severe symptoms
  - Non-albicans species

CDC. 2015 Sexually Transmitted Diseases Treatment Guidelines
VVC Severity Classification

- Recurrent
- Severe symptoms
- Non-albicans species

Remember AD:
Considered
Complicated
Treatment Recommendations

**Uncomplicated**
- OTC intravaginal agents
  - Clotrimazole
  - Miconazole
  - Terconazole
- Oral fluconazole 150 mg once
- Both options have equal efficacy

**Complicated**
- Intravaginal products – Longer duration
- Fluconazole 150 mg every 72 hours x 3 doses
- **Recurrent episodes**: fluconazole 150 mg once weekly x 6 months

CDC. 2015 Sexually Transmitted Diseases Treatment Guidelines
Clinical Question

What are the available treatment options for recurrent vulvovaginal candidiasis when *Candida albicans* has been identified as azole resistant?

- Currently no formal guideline recommendations
- Limited primary literature
Alternative Treatment Options

- Boric Acid Vaginal Capsules
- Nystatin Vaginal Suppository
- Amphotericin B Vaginal Cream ± Flucytosine
Boric Acid Vaginal Capsules

- **Mechanism of Action:**
  - Acidity → cell wall disruption

- **Dose:**
  - 600 mg once or twice daily x 14 days
  - Maintenance: Three time weekly

- **Adverse Effects**
  - Irritation of vaginal epithelium

- **Literature**
  - Retrospective review – 25 recurrent VVC patients
  - Two week therapy: “Majority” boric acid → “invariably” asymptomatic
  - Maintenance therapy based on MIC
  - Mycological cure 9/25 (36%)
    - 3 failures re-cultured → fluconazole susceptible strains
Nystatin Vaginal Suppository

• Mechanism of Action:
  – Binds to the sterol in the cell wall causing cell wall disruption

• Dose:
  – 100,000 units daily x 14 days
  – Maintenance: 7 days before and after menstruation

• Adverse Effects
  – Vaginal pain/burning/itching

• Literature
  – Prospective, open label trial (n=293)
  – Mycological cure – 6 months
    • Fluconazole 70.2% (73/104)
    • Nystatin 80.7% (96/119)
    • P > 0.05
  – Mycological failure: Azole-resistance for any Candida spp.
    • Fluconazole group: 7/7 (1)
    • Nystatin group: 4/9 (2)

C. albicans azole resistance
Amphotericin B Vaginal Cream ± Flucytosine

- **Mechanism of Action:**
  - Binding to ergosterol in the cell wall causing cell wall disruption

- **Dose:**
  - Variable reports
  - 5-10% gel nightly x 14 days

- **Adverse Effects**
  - None reported in case series

- **Literature**
  - 6 patient case series
    - 2 azole resistant *C. albicans*
  - 31 YOF failed fluconazole
    - 14-day course of Ampho B + flucytosine
    - Resolved
  - 44 YOF failed OTC products, fluconazole, and nystatin treatment
    - 14-day course of Ampho B + flucytosine
    - Resolved
Alternative Treatments Overview

Boric Acid Vaginal Capsules
- Compounded
- Less frequent dosing
- Largest amount of studied data

Nystatin Vaginal Suppository
- Compounded
- Frequent dosing
- Familiarity and some data to support use

Ampho B Vaginal Cream ± Flucytosine
- Compounded
- Less clear dosing
- Limited data on efficacy
Recommendation

- First treatment recommendation: Boric acid

- Evaluate at 2 weeks:
  - Maintenance therapy
    - Boric acid
    - Fluconazole based on MIC
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