

PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

Oropharyngeal and Esophageal Candidiasis: A Refresher October 2019

PATIENT CASE

KR is a 68-year-old male recently admitted to hospice with a primary diagnosis of liver cell carcinoma and comorbidities of HIV infection, neuralgia, anxiety, and allergic rhinitis and no known drug allergies. He lives with his sister who is his primary caregiver.

Current medications:

- Abacavir/Lamivudine (Epzicom®) 600/300mg; 1 tablet by mouth every day for HIV infection
- Dexamethasone 4mg; 1 tablet by mouth every day for pain
- Dolutegravir (Tivicay®) 50mg; 1 tablet by mouth every day for infection
- Gabapentin (Neurontin®) 100mg; 1 capsule by mouth three times a day for nerve pain
- Loratadine (Claritin®) 10mg; 1 tablet by mouth every day for allergies
- Lorazepam 0.5mg; 1 tablet by mouth every 4 hours as needed for anxiety
- Methadone 10mg; 1 tablet by mouth every 8 hours for pain
- Ondansetron (Zofran®) 8mg; 1 tablet by mouth every 8 hours as needed for nausea and/or vomiting
- Oxycodone 5mg; 1 tablet by mouth every 4 hours as needed for breakthrough pain
- Ranitidine 150mg; 1 tablet by mouth every day for gastric reflux
- Sennosides/Docusate 8.6/50mg; 2 tablets by mouth every day for constipation (hold for loose stool)

KR exhibits white plaques on the tongue and oropharynx, as well as a feeling he describes as “like cotton in my mouth”. Given KR’s medical conditions and medications, what therapy is best to manage his oropharyngeal candidiasis?

OVERVIEW¹⁻⁴

Oropharyngeal candidiasis, or thrush, is a local infection commonly seen in infants, denture-wearers, patients treated with antibiotics, chemotherapy, or radiation therapy to the head and neck, and those with immunodeficiency states, such as HIV infection and AIDS. Patients treated with inhaled corticosteroids or nasal corticosteroids are also at risk due to inadvertent accumulation of corticosteroid deposited in the oral and nasal mucosa.

The usual causative agent is *Candida albicans*, but other species, including *C. glabrata*, *C. krusei*, and *C. tropicalis*, have been isolated from patients with thrush. When found, these other species grow alongside *C. albicans*, and are the typical culprits of symptomatic infection in most patients. However, in highly immunosuppressed patients, non-albicans species appear to cause the condition.

PRESENTATION⁵⁻⁷

There are 5 types of **oropharyngeal candidiasis**:

- Pseudomembranous - Most common overall and appears as white, curdlike plaques on the buccal mucosa, palate, tongue, and/or the oropharynx
- Atrophic, also called denture stomatitis - Most common in older adults, found under the upper dentures and characterized by erythema without plaques

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- Erythematous – An erythematous patch on the hard and soft palates
- Angular cheilitis – An inflammatory reaction characterized by soreness, erythema, and fissuring at the corners of the mouth
- Mixed – Combination of any of the above types

Many patients with oropharyngeal candidiasis are asymptomatic. When symptoms do occur, patient may describe a cottony feeling in the mouth, loss of taste, burning mouth or tongue, and in some cases, pain and/or soreness during eating and swallowing. Patients who have denture stomatitis usually experience pain.

In addition, immunosuppressed patients with thrush may also have concurrent *Candida* esophageal candidiasis. The symptoms of esophageal candidiasis may be suspected in a patient with evidence of oropharyngeal infection who also complains of hoarseness. Many patients with **esophageal candidiasis** may be asymptomatic however or have one or more of the following symptoms:⁷

- Normal oral mucosa (>50% of patients)
- Dysphagia
- Odynophagia
- Retrosternal pain
- Epigastric pain
- Nausea and vomiting

MANAGEMENT^{1,8-10}

The preferred treatment of oropharyngeal candidiasis differs based on patient-specific factors. The average duration of therapy is 7 to 14 days. For esophageal candidiasis 14 to 21 day-duration of therapy is recommended. When choosing an agent, one must consider drug efficacy for the identified strain and site of infection, severity of infection, ease of administration, anticipated adherence, gastric acidity (which may affect absorption), drug-drug interactions, and cost.

Oropharyngeal candidiasis (7 to 14 day-duration):

- Clotrimazole troches 10 mg; 1 troche dissolved in mouth five times daily
- Miconazole adhesive buccal tablets 50mg; Apply one buccal tablet to the upper gum region, just above the incisor tooth (canine fossa) once daily
- Nystatin suspension; 5ml (500,000units) swish and swallow in mouth and swallow or spit out four times daily
- Fluconazole 100mg to 200mg by mouth daily
- Fluconazole-refractory infections: Voriconazole 200mg by mouth twice daily

Esophageal candidiasis (14 to 21 day-duration):

- Fluconazole 200mg to 400mg by mouth daily
- Fluconazole-refractory infections: Voriconazole 200mg by mouth twice daily OR Itraconazole solution 200mg by mouth daily

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ASSESSMENT AND RECOMMENDATIONS

Patients with HIV infection presenting with their first case of oropharyngeal candidiasis of **mild severity** may use topical agents such as clotrimazole and nystatin. Patients with **moderate to severe** oropharyngeal candidiasis or esophageal candidiasis should be managed with systemic therapy.¹⁰

Studies in patients with HIV and AIDS have compared oropharyngeal candidiasis topical therapy with clotrimazole troches or nystatin to therapy with systemic fluconazole and found that clotrimazole troches had comparable effectiveness to oral fluconazole, whereas nystatin was deemed inferior.^{10,11,12}

Oropharyngeal candidiasis can progress into esophageal candidiasis in immunocompromised patients.⁴ Topical agents such as clotrimazole and nystatin are not recommended for managing esophageal candidiasis. Systemic therapy is a wise choice given the comorbidity of HIV in KR however since he is not exhibiting any symptoms of esophageal involvement at this time, we can initiate therapy with 14-day duration of Fluconazole 200mg by mouth daily, then reassess.

Additionally, fluconazole possesses a number of drug-drug interactions with KR's current regimen that will need to be addressed for the duration of fluconazole therapy:¹³

- Concomitant administration of **fluconazole and ondansetron** increases risk of QT prolongation
 - The combination, if unavoidable, should be continued with extreme caution and careful monitoring
 - It is advisable to elect an alternate antiemetic such as metoclopramide
 - NOTE: Ondansetron, when combined with methadone, also increases risk of QT prolongation and should be continued with the same level of caution as with fluconazole
- Concomitant administration of **fluconazole and methadone** increases risk of QT prolongation and increases the serum concentration of methadone causing increased sedation
 - The combination, if unavoidable, should be continued with extreme caution and careful monitoring
 - Consider empirically reducing the daily dose of methadone by 25% during fluconazole therapy

FOR ADDITIONAL INFORMATION ON THIS TOPIC, PLEASE REVIEW THE FOLLOWING REFERENCES:

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