Good evidence to support efficacy of antifungals for *Candida* treatment in HIV infection

Which antifungal agent is most effective in oropharyngeal candidiasis?

Patton LL, Bonito AJ, Shugars DA. *A systematic review of the effectiveness of antifungal drugs for the prevention and treatment of oropharyngeal candidiasis in HIV-positive patients. Oral Surg Oral Med Oral Pathol* 2001; 92:170–179

Data sources Medline and EMBase and the Cochrane Library to April 2000.

Study selection Articles were only included if they were written in English and the study was performed in humans. A scoring system for quality was used and evidence was graded as good, fair, poor or insufficient. Studies that had no control or comparison group were excluded, as were studies of non-HIV/AIDS populations. Studies reporting mixed-site candidiasis were also excluded if oropharyngeal candidiasis was not reported separately.

Data extraction and synthesis Study design, sampling, study group characteristics, interventions and reported outcomes were extracted.

Results For prevention, six trials met inclusion criteria but there was insufficient evidence to draw conclusions about nystatin, clotrimazole, amphotericin B suspension, ketoconazole or itraconazole. One study demonstrated that nystatin pastilles (at 200 000 and 400 000 IU/day) was effective in the prevention of new or recurrent oropharyngeal candidiasis. There is good evidence, however, that fluconazole is also effective (doses were 50–1000 and 150–200 mg/day). Nausea is a common side effect of fluconazole, but this was reported to be tolerable. For treatment, 12 trials were included. None addressed the efficacy of amphotericin B suspension. Evidence for the effectiveness of the other antifungal agents was good: fluconazole, ketoconazole and itraconazole showed similar efficacy and were more effective than clotrimazole or nystatin, particularly when mycological and relapse rates were considered. Mild adverse events, mainly gastrointestinal problems, rarely resulted in discontinuation of treatment.

Conclusions There is evidence that antifungal drugs are effective in the prevention and treatment of oropharyngeal candidiasis in HIV-infected people. The need remains, however, to improve the evidence base. Larger, better-defined studies are required to address issues such as immunological status, viral load, history of previous candidiasis, past exposure to antifungals, drug interactions and antiretroviral therapy. Studies should also include compliance-monitoring, fungal speciation and susceptibility testing.

Commentary

This finds¹ that a number of agents are available for the prevention and/or treatment of oral *Candida* infection in HIV disease. Systemic azoles such as fluconazole, ketoconazole and itraconazole seem to be of particular benefit. Surprisingly, there are few data suggesting any benefit of topical polyene agents such as nystatin or amphotericin, nor are there any reports of the benefits of chlorhexidine gluconate. Despite the lack of relevant studies, however, a range of agents is available for the prevention or treatment of candidal infection in HIV infection.

A number of questions are raised about healthcare in HIV infection in the 21st century. The merits of antifungal prophylaxis in HIV disease are questionable because few patients, particularly in early HIV infection, have notable complications of oral carriage of *Candida albicans*. Although not mentioned, the use of *Candida* identification in individuals 'not infected with HIV' may also be of limited clinical application because many healthy people harbour *Candida* in the mouth. In addition, oral carriage or clinical manifestation of candidal infection rarely results in any oral symptoms. The needless use of antifungals is highlighted, in particular azoles, leads to the development of azole-resistant *Candida* strains which may then be transmitted within families or to sexual partners, some of whom may be HIV-infected. They correctly state that it is sensible to limit the use of antifungal agents to the treatment of only clinically-evident oral infection.

The advent of highly-active antiretroviral therapy (HAART) has resulted in a fall in the frequency and severity of candidal infection in many treated, HIV-infected people. Therefore, there should be a significant reduction (if only in the developed world) in the need for antifungal therapy — unless of course the frequency of HAART-resistant HIV continues to rise.

Significantly, the majority of HIV infections are found in the developing world, where HAART, itraconazole and fluconazole may not be available. There is a need, therefore, to develop more effective strategies for the treatment of clinically evident *Candida* (and other fungal) infections. HIV-infected individuals in the developing world are not only at risk of rapid development of severe HIV disease as a consequence of malnutrition-associated immunodeficiency, but may carry unusual strains of *Candida* and other fungi. We need to develop simple, cheap and effective strategies for the treatment of candidal infection in such patient groups — particularly children — to minimise the risk of possible systemic *Candida* infection and also avoid the transmission of drug-resistant *Candida* to family members.

As the authors indicate, there are challenges for the developed and developing world in the treatment of HIV-associated fungal infection of the mouth. In view of the limited funding, it seems sensible to focus upon strategies to minimise the development of drug resistance in the developed world, and strategies for simple and effective treatment of fungal infection in the developing world.

Practice point

● A number of agents are available for the prevention and/or treatment of oral *Candida* infection in HIV disease. Because of the dangers of drug resistance, it seems sensible to limit the use of antifungal agents to the treatment of only clinically evident oral candidal infection.

Stephen Porter

Department of Oral Medicine, Eastman Dental Institute, University College London, London, UK

Address of correspondence: Lauren Patton, Department of Dental Ecology, CB7450, School of Dentistry, University of North Carolina, Chapel Hill, NC 27599-7450, USA. E-mail: Lauren_Patton@dentistry.unc.edu

Evidence-Based Dentistry (2003) 4, 14.
doi:10.1038/sj.ebd.6400158