

## Treatment of Recurrent Vulvovaginal Candidiasis

J. DELRENE DAVIS, ARNP, *Department of Family Medicine, University of Washington School of Medicine, Olympia, Washington*

AMY L. HARPER, MLIS, *University of Washington Health Sciences Library, Seattle, Washington*

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### Clinical Question

What is the most effective treatment for recurrent vulvovaginal candidiasis?

### Evidence-Based Answer

A six-month treatment regimen with an antifungal agent decreases the recurrence of vulvovaginal candidiasis. (Strength of Recommendation [SOR]: A, based on good-quality randomized controlled trials [RCTs].) For women in mycologic remission, a six-month treatment regimen with an antifungal agent may result in an additional five to 10 months of clinical cure. (SOR: A, based on good-quality RCTs.) Suitable therapies include oral fluconazole (Diflucan; 150 mg once per week for six months) or oral itraconazole (Sporanox; 200 mg twice per day, one day per month for six months).

### Evidence Summary

Recurrent vulvovaginal candidiasis is defined as at least four documented episodes in the previous 12 months. It affects 5 to 8 percent of reproductive-aged women. Pharmacologic treatments include oral and topical azoles.

In a randomized, double-blind, placebo-controlled study of 343 women, participants were randomized to receive 150 mg of oral fluconazole or placebo once per week for six months.<sup>1</sup> The severity score, ranging from 0 (none) to 9 (severe), was determined based on presence or absence of pruritus, vulvar or vaginal erythema, edema, and excoriation/fissure formation. Evaluation for clinical cure (i.e., score less than 3) or recurrence (i.e., score of 3 or more with positive fungal culture) was performed at six, nine, and 12 months. At randomization, most participants had a negative fungal culture result (91.8 percent of the treatment group versus

86.7 percent of the placebo group;  $P > .05$ ), and all participants had a severity score less than 3. After six months of therapy, 90.8 percent of the treatment group and 35.9 percent of the placebo group were in remission (number needed to treat [NNT] = 2;  $P < .05$ ). Six months after cessation of therapy, 42.9 percent of the treatment group was asymptomatic versus 21.9 percent of the placebo group (NNT = 5; 95% confidence interval, 3 to 10). Median time to clinical recurrence in the treatment group was 10.2 months versus 4.0 months in the placebo group ( $P < .001$ ).

In an earlier study, 114 women with recurrent vulvovaginal candidiasis were randomized to a treatment or observation group.<sup>2</sup> At baseline, both groups were clinically and mycologically free of disease. The treatment group received two doses of itraconazole 12 hours apart on day 4 or 5 of the menstrual cycle for six months. Women from both groups were evaluated at three, six, and 12 months for clinical and mycologic recurrence. The mean time to symptomatic recurrence was 149 days (standard error  $\pm$  6) for the treatment group and 120 days (standard error  $\pm$  6) for the control group ( $P = .003$ ). Remission rates at the end of the initial six months of therapy were 63.6 percent in the treatment group and 35.8 percent in the control group (NNT = 4; 95% confidence interval, 2 to 10). However, six months after completion of therapy, 38.9 percent of women in the treatment group were asymptomatic versus 28.8 percent in the control group, which is not statistically significant.

A prospective, randomized study of 44 women with recurrent vulvovaginal candidiasis compared oral itraconazole with clotrimazole therapy.<sup>3</sup> Women in the itraconazole group received 100 mg twice per

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day for five days, followed by 200 mg twice per week for six months. Women in the clotrimazole group received a 200-mg vaginal tablet daily for five days, followed by 200 mg twice per week for six months. Results from an intention-to-treat analysis showed six-month clinical cure rates of 66.7 percent in the itraconazole group and 100 percent in the clotrimazole group. At 12 months, cure rates were 19 and 35.3 percent, respectively. Clotrimazole vaginal tablets (200 mg) are not available in the United States.

There was no good-quality evidence to support the use of nonpharmacologic therapy, such as consuming yogurt or using intravaginal boric acid, to treat recurrent vulvovaginal candidiasis.

## Recommendations from Others

The Centers for Disease Control and Prevention (CDC) recommends that physicians try to achieve mycologic remission in women with recurrent vulvovaginal candidiasis before starting patients on maintenance therapy. Suitable regimens for mycologic remission include seven to 14 days of topical therapy, or oral fluconazole (100, 150, or 200 mg) every third day for a total of three doses. Maintenance regimens include oral fluconazole (100, 150, or 200 mg) once per week for six months or, if not feasible, 200 mg of topical clotrimazole cream twice per week.<sup>4</sup> The Infectious Diseases Society of America and the American College of Obstetricians and Gynecologists have published guidelines for managing recurrent vulvovaginal candidiasis that mirror those from the CDC.<sup>5,6</sup>

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Address correspondence to J. DelRene Davis, ARNP, at [delrene.davis@providence.org](mailto:delrene.davis@providence.org). Reprints are not available from the authors.

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