Recurrent vulvovaginal candidiasis

Mathieos Belayneh Evan Sehn Christina Korownyk MD CCFP

Clinical question

What is the most effective management for women with recurrent vulvovaginal candidiasis (≥4 episodes within 1 year)?

Bottom line

Prophylaxis with 6 months of azole therapy will reduce relapse to 9% to 19% of women compared with 50% to 64% with placebo (1 fewer woman would relapse for every 2 to 4 treated). However, efficacy declines after therapy cessation and clinical cure remains elusive. Limited evidence suggests women might prefer episodic over maintenance therapy.

Evidence

Two double-blind RCTs of 373[1] and 64 women[2] with symptoms and culture-confirmed recurrent vulvovaginitis compared 150 mg of oral fluconazole weekly for 6 months (after an initial 150 mg of oral fluconazole every 72 hours for 3 days) with placebo:

- There was a statistically significant difference in clinical relapse rate:
  -After 6 months' treatment,[1,2] 9% to 19% relapsed versus 50% to 64% (number needed to treat [NNT]=2 to 4).
- At the 12-month follow-up,[1] 57% had relapsed versus 78% (NNT=5). There was no significant difference in relapse in the smaller study,[2] and no increase in resistance in either study.[1,2]
- There was 1 case of "mild" elevation of liver enzymes that did not require treatment discontinuation.[1]
- Analysis only included those compliant with treatment.[1]

Two RCTs examined 400 mg of oral itraconazole monthly (N=114)[3] and a monthly 500-mg clotrimazole vaginal suppository (N=62)[4] versus placebo for 6 months.

- Statistically significant difference in clinical relapse rate: 30% to 36% versus 64% to 79%, NNT=3 to 4.
- No longer significant at the 12-month follow-up.[3,4]

One observational study of 136 women individualized decreasing doses (200 mg of fluconazole 3 times a week, weekly for 2 months, biweekly for 4 months, then monthly for 6 months) based on clinical symptoms[5]:

- There was a 30% clinical relapse rate during 12 months of treatment and a 45% rate at the 18-month follow-up.

Context

- Studies of alternative therapies, such as probiotics or homeopathy, are of poor quality and have mixed results.[6]
- Limited evidence suggests no significant difference among azoles in acute or recurrent *Candida albicans* vulvovaginitis.[7]
- *Candida albicans* causes 90% of vulvovaginal candidiasis, followed by *Candida glabrata,* which is azole resistant.[8]
- A small trial (54 women) showed that treating male sexual partners with antifungals does not reduce relapse.[9]
- A randomized crossover trial of 23 women reported 74% versus 14% prefer to treat each episode empirically versus maintenance therapy.[10]

Implementation

Only about one-third of women correctly self-diagnose vulvovaginal candidiasis.[11] Yeast culture might be considered if the patient has recurrent infection, has treatment failure, or is immunocompromised. Small studies comparing boric acid (600 mg intravaginally daily for 7 to 14 days) with intravaginal nystatin or oral fluconazole suggest it has limited efficacy, particularly against *C glabrata*.[12] Boric acid requires pharmacy compounding and might cause vulvovaginal irritation. There are no RCTs examining boric acid as prophylaxis.

Mr Belayneh is a medical student and **Mr Sehn** is a Doctor of Pharmacy student, both at the University of Alberta in Edmonton. **Dr Korownyk** is Associate Professor in the Department of Family Medicine at the University of Alberta.

Competing interests
None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

References

1. Sobel JD, Wiesenfeld HC, Martens M, Danna P, Hooton TM, Rompalo A, et al. Maintenance fluconazole for recurrent vulvovaginal candidiasis. *N Engl J Med* 2004;351(9):876-83.
2. Bolouri F, Moghadami Tabrizi N, Davari Tanha F, Niroomand N, Azmoodeh A, Emami S, et al. Effectiveness of fluconazole for suppressive maintenance therapy in patients with RVVC: a randomized placebo-controlled study. *Iran J Pharm Res* 2009;8(4):307-13.
3. Spinillo A, Colonna L, Piazzi G, Baltaro F, Monaco A, Ferrari A. Managing recurrent vulvovaginal candidiasis. Intermittent prevention with itraconazole. *J Reprod Med* 1997;42(2):83-7.
4. Roth AC, Milsom I, Forssman L, Wåhlén P. Intermittent prophylactic treatment of recurrent vaginal candidiasis by postmenstrual application of a 500 mg clotrimazole vaginal tablet. *Genitourin Med* 1990;66(5):357-60.
5. Donders G, Bellen G, Byttebier G, Verguts L, Hinoul P, Walckiers R, et al. Individualized decreasing-dose maintenance fluconazole regimen for recurrent vulvovaginal candidiasis (ReCiDiF trial). *Am J Obstet Gynecol* 2008;199(6):613.e1-9.
6. Falagas ME, Betsi GI, Athanasiou S. Probiotics for prevention of recurrent vulvovaginal candidiasis: a review. *J Antimicrob Chemother* 2006;58(2):266-72.
7. Pitsouni E, Iavazzo C, Falagas ME. Itraconazole vs fluconazole for the treatment of uncomplicated acute vaginal and vulvovaginal candidiasis in nonpregnant women: a metaanalysis of randomized controlled trials. *Am J Obstet Gynecol* 2008;198(2):153-60.
8. Sobel JD. Recurrent vulvovaginal candidiasis. *Am J Obstet Gynecol* 2016;214(1):15-21.
9. Fong IW. The value of treating the sexual partners of women with recurrent vaginal candidiasis with ketoconazole. *Genitourin Med* 1992;68(3):174-6.
10. Fong IW. The value of prophylactic (monthly) clotrimazole versus empiric self-treatment in recurrent vaginal candidiasis. *Genitourin Med* 1994;70(2):124-6.
11. Ferris DG, Nyirjesy P, Sobel JD, Soper D, Litaker MS. Over-the-counter antifungal drug misuse associated with patient-diagnosed vulvovaginal candidiasis. *Obstet Gynecol* 2002;99(3):419-25.
12. Ray D, Goswami R, Banerjee U, Dadhwal V, Goswami D, Mandal P, et al. Prevalence of *Candida glabrata* and its response to boric acid vaginal suppositories in comparison with oral fluconazole in patients with diabetes and vulvovaginal candidiasis. *Diabetes Care* 2007;30(2):312-7.

Tools for Practice articles in *Canadian Family Physician (CFP)* are adapted from articles published on the Alberta College of Family Physicians (ACFP) website, summarizing medical evidence with a focus on topical issues and practice-modifying information. The ACFP summaries and the series in *CFP* are coordinated by **Dr G. Michael Allan**, and the summaries are co-authored by at least 1 practising family physician and are peer reviewed. Feedback is welcome and can be sent to **toolsforpractice@cfpc.ca**. Archived articles are available on the ACFP website: **www.acfp.ca**.