

Review: Oral and intravaginal agents are equally effective for treatment of uncomplicated vulvovaginal candidiasis

Watson MC, Grimshaw JM, Bond CM, Mollison J, Ludbrook A. Oral versus intra-vaginal imidazole and triazole anti-fungal treatment of uncomplicated vulvovaginal candidiasis (thrush). *Cochrane Database Syst Rev.* 2001;(4):CD002845 (latest version 28 May 2001).

QUESTION

Are oral and intravaginal antifungal agents equally effective, safe, and cost-effective for uncomplicated vulvovaginal candidiasis?

DATA SOURCES

Randomized controlled trials (RCTs) published in any language were identified by searching the Cochrane Controlled Trials Register (CENTRAL/CCTR), the Cochrane Collaboration Sexually Transmitted Disease Group Specialised Register of Controlled Trials, EMBASE/Excerpta Medica (1980 to January 2000), and MEDLINE (January 1985 to May 2000). Reference lists of each trial were reviewed, and U.K. manufacturers of antifungal agents were contacted.

STUDY SELECTION

Trials were selected if they included women ≥ 16 years of age with mycologically confirmed acute vulvovaginal candidiasis (< 4 episodes in 12 mo) and compared ≥ 1 oral antifungal agent with an intravaginal antifungal agent. Trials were excluded if they included only participants who were HIV-positive, immunocompromised, pregnant, breast-feeding, or diabetic.

DATA EXTRACTION

Data were extracted on the type, dose, frequency, and duration of antifungal treat-

ment; setting; participants; and outcome measures. Main outcomes were short- and long-term clinical cure rates. Secondary outcomes included mycological cure rates (culture), incidence of adverse reactions, and cost-effectiveness. Individual studies were assessed for methodologic quality (random allocation, concealment of allocation, adequate follow-up, and blinding of outcome assessors).

MAIN RESULTS

17 RCTs reporting 19 comparisons were included in the analysis. The trials assessed 2 oral agents (fluconazole and itraconazole) and 4 intravaginal agents (clotrimazole, econazole, miconazole, and terconazole).

Meta-analyses were done using a random-effects model; the denominator for analysis was the number of randomized patients who had positive cultures for yeast before antifungal treatment began. Length of follow-up was classified as short term (5 to 15 d) and long term (2 to 12 wk). Oral and intravaginal antifungal agents did not differ for clinical cure at short-term (9 comparisons, $n = 1247$, 80% vs 80%) or long-term (7 comparisons, $n = 836$, 83% vs 82%) follow-up or for mycological cure at short-term (17 comparisons, $n = 2239$, 83% vs 82%) or long-term

(14 comparisons, $n = 1711$, 72% vs 66%) follow-up. Sensitivity analyses based on all randomized participants, blinding, and the proportion of patients followed did not change the effect sizes for any of the outcomes.

11 trials reported on adverse reactions. Intravaginal agents were associated with such local reactions as irritation, burning, and pruritis and such systemic effects as headache, whereas oral agents were associated with such systemic effects as gastrointestinal effects and headache. Data were insufficient to compare the relative safety of oral and intravaginal agents. No trials of the relative cost-effectiveness of oral and intravaginal agents were found.

CONCLUSIONS

Oral and intravaginal agents are equally effective in the treatment of uncomplicated vulvovaginal candidiasis. Insufficient data exist on adverse effects and cost-effectiveness of the 2 types of treatment.

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COMMENTARY

The findings of the systematic review by Watson and colleagues support the general view of treatment for uncomplicated vulvovaginal candidiasis. The review did not identify any studies that compared single oral doses of antifungal agents with multidose oral antifungals, leaving this issue unexplored. Similarly, single topical applications were not compared with multidose topical applications. Efficacy—the cure rate under ideal clinical conditions—may differ from effectiveness—the cure rate in the real world (e.g., forgotten applications and misapplications). The authors did not assess whether the efficacy and effectiveness of the antifungal agents measured in industry-sponsored trials differed from those measured in non-industry-sponsored trials.

Most vaginal discharges are caused by one of 3 organisms: a fungus (*Candida*), a protozoan (*Trichomonas*), and a combination of anaerobic and aerobic bacteria. Conditions caused by these organisms occur at different frequencies dependent on the population. In a middle-class U.S. population, bacterial vaginosis occurs 50% of the time, and candidiasis and trichomonas each occur 25% of the time (1).

Concurrent partner treatment does not improve a woman's cure rate (2, 3), but in the approximately 5% of women with recurrent infection (4), partner treatment to eradicate the intestinal reservoir of *Candida* has proved efficacious (5).

The 17 RCTs were done in Europe ($n = 9$), the United States ($n = 5$), Japan ($n = 1$), Thailand ($n = 1$), and Africa ($n = 1$). The use of antifungal agents for vulvovaginal candidiasis varies by cultural habits, effectiveness, cost-effectiveness, safety, and preferences characteristic of the given population.

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