FPIN's Clinical Inquiries

Probiotics to Augment Antifungal Treatment of Vulvovaginal Candidiasis

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Clinical Question

How effective are probiotics for augmenting antifungal treatment of vulvovaginal candidiasis?

Evidence-Based Answer

Adding probiotics (typically *Lactobacillus* species) to antifungal therapy for vulvovaginal candidiasis improves short-term cure rates by 14% and reduces one-month relapse rates by 66%. (Strength of Recommendation [SOR]: B, based on a meta-analysis of low-quality randomized controlled trials [RCTs].) Adding probiotics to antifungal therapy for women with recurrent vulvovaginal candidiasis may improve long-term cure rates over three to six months. (SOR: C, based on a small RCT that conflicted with low-quality RCTs.)

Evidence Summary

A 2017 Cochrane review of five low-quality RCTs (n = 695) found that adding probiotics to antifungal regimens increased the short-term clinical cure rate in women with vulvovaginal candidiasis.[1] The studies included nonpregnant Chinese and Iranian women 16 to 50 years of age. The diagnosis of vulvovaginal candidiasis was initially made symptomatically, then confirmed by microscopy. Women with recurrent vulvovaginal candidiasis, diabetes mellitus, immunosuppression, or evidence of coinfections were excluded. Patients were randomized to antifungal therapy alone or antifungals plus probiotics (vaginal capsules in four studies and oral capsules in one study; capsules contained single or multiple strains of *Lactobacillus* species [*L. delbrueckii, L. casei, L. rhamnosus,* or *L. acidophilus*], *Streptococcus* species [*S. thermophilum* or *S. faecalis*], and/or *Bifidobacterium* species [*B. breve* or *B. longum*]). Short-term clinical cure was defined as resolution of symptoms plus absence of *Candida* on microbiologic culture within 14 days. Probiotics significantly improved cure rates (relative risk [RR] = 1.14; 95% CI, 1.05 to 1.24). Three of the RCTs (n = 388) found that adding probiotics to antifungal therapy reduced the relapse rate at one month (RR = 0.34; 95% CI, 0.17 to 0.68) compared with antifungal therapy alone. Relapse was defined as symptom recurrence with positive microscopy or vaginal culture.

A double-blind, placebo-controlled RCT (n = 48) found that probiotics reduced recurrent symptoms of vulvovaginal itching and discharge.[2] The study included white women (average age: 35) with a history of recurrent vulvovaginal candidiasis who had symptoms of acute vulvovaginal candidiasis and positive cultures for *Candida*. This study had two treatment phases. In the induction phase, the treatment group was given

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standard antifungal therapy plus an oral probiotic containing *L. acidophilus, L. rhamnosus,* and lactoferrin. The probiotic was continued for eight days after the final antifungal dose. In the maintenance phase, the treatment group was given two capsules containing *Lactobacillus* and lactoferrin each day for five days, then one per day for 10 days per month during the premenstrual period. Women in the treatment group reported less itching and discharge compared with the control group (no itching: 70.8% vs. 8.3% at three months and 83.3% vs. 0% at six months, respectively; $P < .01$ for both; no discharge: 66.7% vs. 8.3% at three months and 70.8% vs. 20.8% at six months; $P < .01$ for both). The probiotic also reduced recurrence rates (33.3% with probiotic vs. 91.7% at three months; $P < .01$; and 29.2% vs. 100% at six months; $P < .01$).

An earlier RCT (n = 172) that was included in the 2017 Cochrane review but rated very low quality found no change in the clinical cure rate at three months when vaginal probiotic capsules were added to antifungal therapy (RR = 1.30; 95% CI, 1.00 to 1.70).[1] The study included women with recurrent vulvovaginal candidiasis and defined long-term clinical cure as symptomatic improvement with no evidence of fungal infection on culture and examination one month after treatment.

A low-quality RCT (n = 93) published in 2018 found that probiotics did not improve symptoms of recurrent vulvovaginal candidiasis in Romanian women.[3] Investigators found no difference in vaginal redness and swelling at 45 and 90 days.

The 2017 Cochrane review included low-quality RCTs that evaluated rates of adverse effects with probiotic use.[1] These studies found no differences in serious (two RCTs; n = 440; RR = 0.80; 95% CI, 0.22 to 2.94) or nonserious effects (seven RCTs; n = 906; RR = 0.90; 95% CI, 0.48 to 1.70). Investigators defined serious adverse effects as death, internal organ injury, and severe skin and mucosal injury. Nonserious effects included vomiting; diarrhea; abdominal pain; abnormal urination; pelvic cramps; paresthesia; rhinorrhea; headache; dizziness; fever; chills; and vaginal burning, stinging, itching, or irritation.

Recommendations from Others

The Society of Obstetricians and Gynaecologists of Canada published recommendations in 2015 that did not specifically address the addition of probiotics to standard antifungal therapy for vulvovaginal candidiasis, but stated that evidence was limited for probiotic treatment of bacterial vaginosis.[4] A 2015 German guideline on the treatment of vulvovaginal candidiasis recommended that *Lactobacillus*-containing probiotics be examined in future studies because of encouraging initial results.[5]

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References

1. Xie HY, Feng D, Wei DM, et al. Probiotics for vulvovaginal candidiasis in non-pregnant women. *Cochrane Database Syst Rev.* 2017;(11):CD010496.
2. Russo R, Superti F, Karadja E, et al. Randomised clinical trial in women with recurrent vulvovaginal candidiasis: efficacy of probiotics and lactoferrin as maintenance treatment. *Mycoses.* 2019;62(4):328-335.
3. Vladareanu R, Mihu D, Mitran M, et al. New evidence on oral *L. plantarum* P17630 product in women with history of recurrent vulvovaginal candidiasis (RVVC): a randomized double-blind placebo-controlled study. *Eur Rev Med Pharmacol Sci.* 2018;22(1):262-267.
4. Van Schalkwyk J, Yudin MH; Infectious Disease Committee. Vulvovaginitis: screening for and management of trichomoniasis, vulvovaginal candidiasis, and bacterial vaginosis. *J Obstet Gynaecol Can.* 2015;37(3):266-274.
5. Mendling W, Brasch J, Cornely OA, et al. Guideline: vulvovaginal candidosis (AWMF 015/072), S2k (excluding chronic mucocutaneous candidosis). *Mycoses.* 2015; 58(suppl 1):1-15. ■