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Probiotics for vulvovaginal candidiasis in non-pregnant women (Review) Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



# [Intervention Review]

# Probiotics for vulvovaginal candidiasis in non-pregnant women

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# ABSTRACT

#### Background

Vulvovaginal candidiasis (VVC) is estimated to be the second most common form of infection after bacterial vaginosis. The ability of probiotics in maintaining and recovering the normal vaginal microbiota, and their potential ability to resist *Candidas* give rise to the concept of using probiotics for the treatment of VVC.

# Objectives

To assess the effectiveness and safety of probiotics for the treatment of vulvovaginal candidiasis in non-pregnant women.

# Search methods

We searched the following databases to October 2017: Sexually Transmitted Infections Cochrane Review Group's Specialized Register, CENTRAL, MEDLINE, Embase and eight other databases. We searched in following international resources: World Health Organization International Clinical Trials Registry Platform, ClinicalTrials.gov, Web of Science and OpenGrey. We checked specialty journals, reference lists of published articles and conference proceedings. We collected information from pharmaceutical companies and experts in the field.

#### **Selection criteria**

Randomized controlled trials (RCT) using probiotics, alone or as adjuvants to conventional antifungal drugs, to treat VVC in non-pregnant women. Trials recruiting women with recurrent VVC, coinfection with other vulvovaginal infections, diabetes mellitus, immunosuppressive disorders or taking immunosuppressant medication were ineligible for inclusion. Probiotics were included if they were made from single or multiple species and in any preparation type/dosage/route of administration.

#### Data collection and analysis

Two review authors independently assessed trials for eligibility and quality and extracted data. We resolved any disagreements through consensus. The quality of the evidence was assessed using the GRADE approach.

#### **Main results**

Ten RCTs (1656 participants) met our inclusion criteria, and pharmaceutical industry funded none of these trials. All trials used probiotics as adjuvant therapy to antifungal drugs. Probiotics increased the rate of short-term clinical cure (risk ratio (RR) 1.14, 95% confidence interval (CI) 1.05 to 1.24, 695 participants, 5 studies, low quality evidence) and mycological cure (RR 1.06, 95% CI 1.02 to 1.10, 969 participants, 7 studies, low quality evidence) and ecreased relapse rate at one month (RR 0.34, 95% CI 0.17 to 0.68, 388 participants, 3 studies, very low quality evidence). However, this effect did not translate into a higher frequency of long-term clinical cure (one month after treatment: RR

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1.07, 95% CI 0.86 to 1.33, 172 participants, 1 study, very low quality evidence; three months after treatment: RR 1.30, 95% CI 1.00 to 1.70, 172 participants, one study, very low quality evidence) or mycological cure (one month after treatment: RR 1.26, 95% CI 0.93 to 1.71, 627 participants, 3 studies, very low quality evidence; three months after treatment: RR 1.16, 95% CI 1.00 to 1.35, 172 participants, one study, very low quality evidence). Probiotics use did not increase the frequency of serious (RR 0.80, 95% CI 0.22 to 2.94; 440 participants, 2 studies, low quality evidence). We found no eligible RCTs for outcomes as time to first relapse, need for additional treatment at the end of therapy, patient satisfaction and cost effectiveness.

#### **Authors' conclusions**

Low and very low quality evidence shows that, compared with conventional treatment, the use of probiotics as an adjuvant therapy could increases the rate of short-term clinical and mycological cure and decrease the relapse rate at one month but this did not translate into a higher frequency of long-term clinical or mycological cure. Probiotics use does not seem to increase the frequency of serious or non-serious adverse events. There is a need for well-designed RCTs with standardized methodologies, longer follow-up and larger sample size.

# PLAIN LANGUAGE SUMMARY

#### Probiotics for vulvovaginal candidiasis in non-pregnant women

#### Question

In this Cochrane Review, we assessed the effect and safety of probiotics for the treatment of vulvovaginal candidiasis (VVC) in non-pregnant women compared with conventional antifungal drugs, or probiotics used to change the effects of conventional antifungal drugs.

#### Background

The condition of VVC occurs because of an imbalance in the normal vaginal microorganism habitat (microbiota). It is characterized by a decrease of a type of bacteria called lactobacilli and a concomitant overgrowth of a fungus called *Candida*. Although treatments for VVC by conventional antifungal drugs are quite effective at providing clinical cure (no apparent vaginal symptoms), there is an increasing in resistance to the drugs and recurrence of VVC. Conventional antifungal drugs can also cause many side effects. Probiotics are microorganisms that are believed to provide health benefits when consumed. The ability of probiotics in maintaining and recovering the normal vaginal microbiota, and their potential ability to resist *Candidas* gives rise to the concept of using probiotics for the treatment of VVC. We wanted to find out whether using probiotics could be useful in treating VVC in non-pregnant women without high risk or side effects.

#### **Study characteristics**

We searched evidence up to October 2017 and included 10 clinical trials with 1656 participants. The trials lasted between three months and five years. All trials used at least one laboratory method for diagnosis. Four trials compared vaginal suppository (solid medicine inserted directly into the vagina) or tablet of clotrimazole (antifungal medicine) plus vaginal capsules of probiotics with vaginal suppository or tablet of clotrimazole alone. Three trials compared vaginal suppository of miconazole (antifungal medicine) plus vaginal capsules of probiotics with vaginal suppository of miconazole alone. Two trials compared oral fluconazole (antifungal medicine) plus oral capsules of probiotics with oral fluconazole plus oral capsules of placebo (pretend treatment). One trial compared oral fluconazole and vaginal fenticonazole (antifungal medicines) with oral fluconazole plus vaginal fenticonazole plus probiotic.

#### **Key results**

Compared with conventional antifungal drugs used alone, probiotics as adjuvant therapy could enhance their effect in improving the rate of short-term (within five to 10 days) clinical cure, short-term mycological cure (no abnormal laboratory results) and relapse at one month (recurrence of problems), but does not seem to influence the rate of long-term (within one to three months) clinical cure, long-term mycological cure, serious and non-serious side events.

However, because of the low quality of evidence available, there is insufficient evidence for the use of probiotics as adjuvants to conventional antifungal medicines or used alone for the treatment of VVC in non-pregnant women.

#### **Quality of the evidence**

The quality of the evidence was low or very low in this review, so we have very little confidence in the results.