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## Effect of Probiotics on Recurrent Vaginal Candidiasis Infection

 Zeynep Ayaz

Department of Family Medicine, Mersin Mezitli Public Health Center, Mersin, Turkey

### ABSTRACT

Vaginal candidiasis is the second most common after bacterial vaginosis. It is accepted that 5%–10% of women with vaginal candidiasis are exposed to recurrent infections. For the case to be considered recurrent, it must have had at least four symptomatic attacks within 12 months. In the treatment of recurrent vulvovaginal candidiasis, suppressive and preventive treatment of episodes is recommended rather than individual treatment of episodes. Increasing drug resistance and drug side effects that may develop in long-term use make it necessary to consider alternative options in the treatment of recurrent vaginitis. Probiotics are nonpathogenic microorganisms that regulate microbial balance, especially in the gastrointestinal tract, and they can also be considered as a useful alternative in the treatment of recurrent candida. These agents regulate the immunore-sponse of the host by reducing the invasion and colonization of pathogenic microorganisms by lowering the pH in their region. The aim of this review was to investigate the effectiveness of local probiotic use following conventional topical azole treatment on preventing recurrence of recurrent vaginal candida infections.

**Keywords:** Candidiasis, vulvovaginal candidiasis, probiotics



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#### Address for correspondence:

Dr. Zeynep Ayaz. Department of Family Medicine, Mersin Mezitli Public Health Center, Mersin, Turkey

Phone: +90 505 678 89 59

#### E-mail:

zeynepayaz170@gmail.com

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### INTRODUCTION

Vaginal candidiasis is the second most common after bacterial vaginosis.<sup>[1]</sup> Its incidence is 118–200/100 000 women, and it has been reported that 75% of women of reproductive age have an attack of vulvovaginal candidiasis and half of this infection can be seen again.

The causative agent of vulvovaginitis caused by candida is usually *Candida albicans*, and this microorganism is often saprophytic in the skin, intestine, vagina, and oropharynx.<sup>[2]</sup> It is not sexually transmitted. Symptomatic vaginitis occurs with excessive proliferation of the agent.<sup>[3]</sup> The use of antibiotics, corticosteroids, and oral contraceptives, uncontrolled diabetes, intensive colonization in the gastrointestinal system, use of synthetic underwear, and vaginal douching cause symptomatic vaginal candidiasis. It usually involves the vulvovaginal area. The most common symptoms are itching, dysuria, dyspareunia, and rarely local pain. The skin may be erythematous, slightly edematous, and often eroded or have a normal appearance. Vaginal discharge is odorless, thick, white, and clumpy.

Although the diagnosis can be made microscopically by examining the vaginal discharge sample and seeing the hyphae, it is usually made by symptoms and examination findings.<sup>[4]</sup> Although culture is not applied routinely, it should be performed in cases that cannot be diagnosed clinically and microscopically or who show chronic recurrence.<sup>[5]</sup> Treatment is successful in more than 80% of cases with all antimycotic agents. It is reported that the use of all vaginal and oral preparations has a similar effect.<sup>[6]</sup>

## Recurrent Vaginitis

It is accepted that 5%–10% of women with vaginal candidiasis are exposed to recurrent infections.<sup>[7,8]</sup> For the case to be considered recurrent, it must have had at least four symptomatic attacks within 12 months.<sup>[7]</sup> Recurrent vaginal candidiasis is associated with frequent and prolonged symptoms. It has a negative impact on the quality of life and mental status of women.<sup>[9]</sup> The most important causes of recurrent vulvovaginal candidiasis (RVVC) are the development of resistance to drugs used in the treatment of candida vaginitis, broad-spectrum antibiotics, oral contraceptives, steroids and immunosuppressant drugs, and over-the-counter drugs that disrupt the flora in favor of pathogenic microorganisms. Uncontrolled use of antifungals has been reported.<sup>[7,10]</sup> In addition, recurrent candida vaginitis is more common in uncontrolled diabetes, and *Candida glabrata* has been found to be the most frequently isolated causative agent in type 2 diabetics and postmenopausal women.<sup>[11]</sup>

In the treatment of RVVC, suppressive and preventive treatment of episodes is recommended rather than individual treatment of episodes.<sup>[12]</sup> In this treatment, it is recommended to use fluconazole orally at 150 mg/day, three doses at 72 h apart, followed by a single dose of 150 mg once a week for at least 6 months. Alternative treatments are topical azole for 7–14 days or 150 mg oral fluconazole on days 1, 4, and 7; following topical or oral azole treatment for 10–14 days, the use of 150 mg fluconazole once a week for 6 months or 200 mg clotrimazole vaginal cream twice a week. The development of drug resistance and possible side effects of existing antifungals restricts its use for prophylaxis.<sup>[13]</sup> Increasing drug resistance and drug side effects that may develop in long-term use make it necessary to consider alternative options in the treatment of recurrent vaginitis.

## Probiotics and Their Mechanism of Action

The term probiotic means “for life” and is derived from Greek. It has become popular thanks to the use of Nobel Prize-winning scientist E. Metchnikoff’s fermented dairy products in the treatment of gastrointestinal tract diseases.<sup>[14,15]</sup> It has been suggested that Bulgarian villagers, who consume large amounts of probiotic foods, live longer, and this effect is due to probiotic bacteria found in fermented dairy products. Probiotics are nonpathogenic microorganisms that regulate microbial balance, especially in the gastrointestinal tract. It contains microorganisms such as *Saccharomyces boulardii*, *Lactobacillus*, and *Bifidobacterium* species. These agents regulate the immune response of the host by reducing the invasion and colonization of patho-

genic microorganisms by lowering the pH in their region. The main probiotic bacteria species are summarized in Table 1.

Probiotic products, on the other hand, are produced by Haveanar and Huist Veld in a sufficient number of living microorganisms that change the microflora (by implantation and colonization) in a region of the host.<sup>[16]</sup> Probiotics acts in the following ways; they produce antibacterial agents; strengthen the mucosal barrier; increase intestinal motility; increase monocyte, macrophage, and polymorphonuclear leucocyte levels; increase phagocytic activity; increase IgA and IgG levels; and prevent the growth of pathogenic bacteria. They show by neutralizing the toxins produced by pathogens. As well as products such as yogurt, milk, and ayran in the market, they are also found in baby milk and food, in medication such as capsule, liquid, sachet, and ovule. Although there are positive results in the use of probiotics in treatment, infections such as septicemia, endocarditis, and mediastinitis have been reported, especially in people with immune deficiency, organ failure, and some intestinal diseases.<sup>[17]</sup> Therefore, risk groups should be considered in the use of probiotics.

## Use of Probiotics in the Treatment of Vaginal Candidiasis and Prevention of Recurrence

As probiotics contain lactobacilli, which constitute the most important group of natural vaginal flora, it has been shown that it replaces the vaginal flora and reduces vaginal PH with components such as bacteriocin, lactic acid, and hydrogen peroxide and supports mucosal immunity through an immunomodulation mechanism, thus preventing pathogen candida colonization and thus clinical candida vaginitis.<sup>[18,19]</sup> It has been shown to correct their symptoms. In this context, probiotics can also be considered as a useful alternative in the treatment of recurrent candida. Although some studies conducted with probiotics, most of which contain *Lactobacillus acidophilus*, show that these

**Table 1.** Main probiotic bacteria species

<i>Lactobacillus</i> species	<i>Bifidobacterium</i> species	<i>Bacillus</i> species
<i>L. delbrueckii</i>	<i>B. bifidum</i>	<i>B. subtilis</i>
<i>L. rhamnosus</i>	<i>B. longum</i>	<i>B. pumilus</i>
<i>L. acidophilus</i>	<i>B. thermophilum</i>	<i>B. licheniformis</i>
<i>Bacteroides</i> species	<i>Streptococcus</i> species	Molds and yeast
<i>B. suis</i>	<i>S. salivarius</i>	<i>Aspergillus niger</i>
<i>B. amylophilus</i>	<i>S. intermedius</i>	<i>Saccharomyces cerevisiae</i>
<i>B. capillus</i>	<i>S. thermophilus</i>	<i>Aspergillus oryzae</i>

products prevent recurrence of urogenital *C. albicans* infections and reduce the recurrence rate. Although there is no definitive protocol for the use of probiotics in vaginal candidiasis, in some studies, oral probiotics, used for 15 days for 6 months and 15 days are interrupted, once a month or local (as a vaginal capsule or gel) for 10 days, showed significant improvement in the relief of symptoms and signs.<sup>[20,21]</sup> Probiotic products will be used in this regard due to the variety and qualitative differences, duration of use of probiotics, and differences in the factors that cause RVVC and patient characteristics.<sup>[22]</sup> In a national study, the frequency of vaginal candidiasis in symptomatic women was reported to be 16% and 75% of the isolated candida strains were *C. albicans*.<sup>[23]</sup> The frequency of *C. glabrata* was 14%. In the systematic review of Güzel et al., it was reported that the frequency of *C. albicans* in vaginal cultures is 50%, and this frequency is lower than the rates reported in Europe and North America. The rates of non-*candida albicans* are reported to be between 42.9% and 49.6%.<sup>[24]</sup> It was thought that resistant candida vaginitis is seen more frequently in Turkey, but there is no national research on the treatment of resistant cases.

## CONCLUSION

The aim of this review was to investigate the effectiveness of local probiotic use following conventional topical azole treatment on preventing recurrence of recurrent vaginal candida infections. Although current drug regimens treat vaginal candidiasis, they may be insufficient to prevent a recurrence. At this point, different methods are used and probiotics come to the fore by regulating the vaginal biota. More studies are needed to determine whether they can be included in the new treatment algorithm as well as treating relapse.

## Disclosures

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