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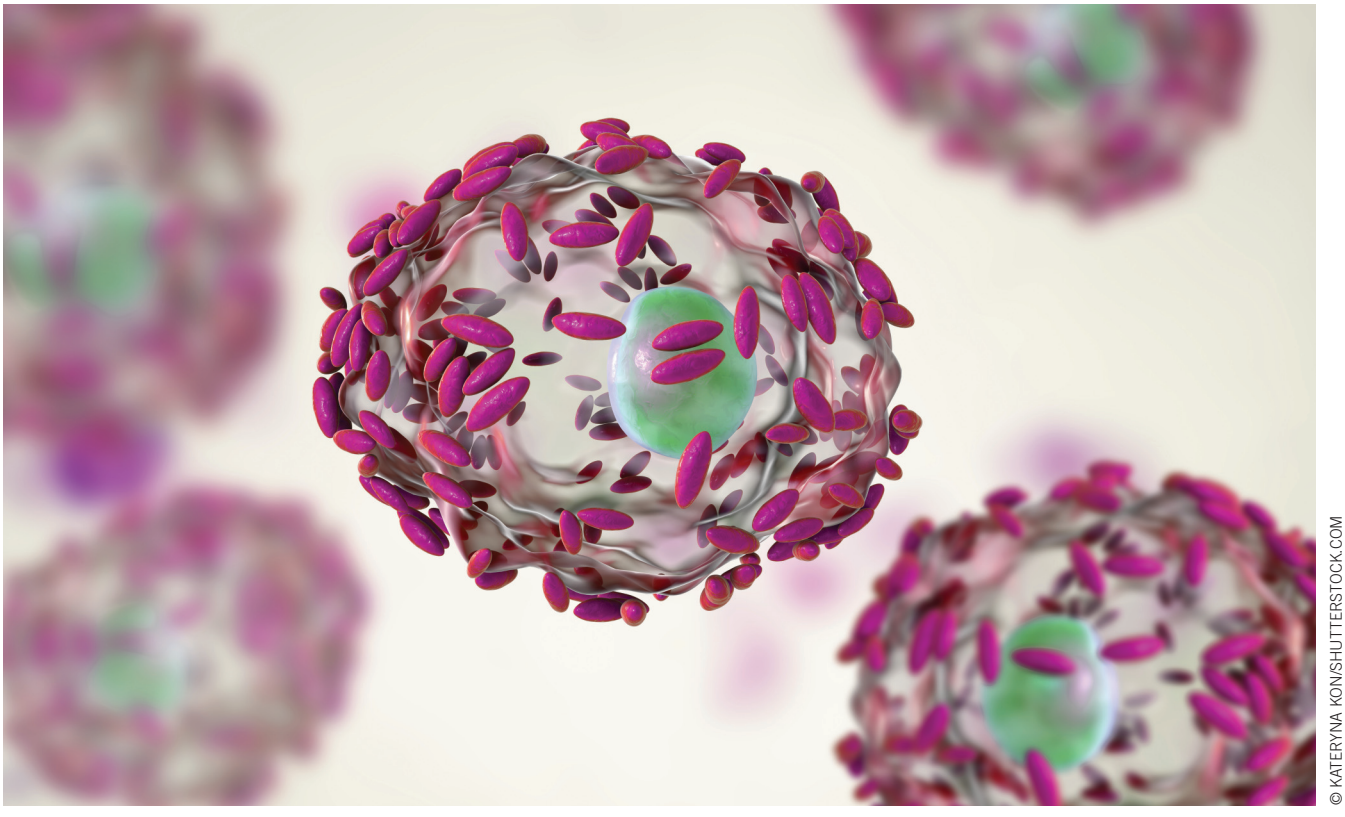

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Probiotics for preventing recurrent bacterial vaginosis

Lauren Webb, DMSc, PA-C

ABSTRACT

Multiple studies have shown that oral or vaginal probiotics can effectively treat and prevent recurrent bacterial vaginosis. The dose, route, and treatment protocols vary greatly between studies, but many have shown a statistically significant reduction in the rate of recurrence of bacterial vaginosis. Further research is needed to determine the adequate dose, specific probiotic, optimal duration, and route of administration, with or without antibiotics.

Keywords: bacterial vaginosis, prevention, recurrent, probiotics, *Lactobacillus,* microbiome

Learning objectives

- Describe the pathophysiology of bacterial vaginosis.
- List the risk factors for contracting bacterial vaginosis.
- Describe the signs and symptoms leading to the diagnosis of bacterial vaginosis.
- List traditional and probiotic regimens that can be used in the treatment of bacterial vaginosis.

Bacterial vaginosis is a common vaginal infection, occurring in 30% of women of childbearing age in the United States, and recurring in 20% to 30% of these women after initial treatment.[1] The condition typically is caused by an overgrowth of normal vaginal flora, such as the Gram-negative bacterium *Gardnerella vaginalis*, and is seen concurrently with a diminished amount of normal vaginal lactobacilli.[2] Because vaginal lactobacilli help to maintain a normal vaginal pH, a diminished lactobacillus level allows for overgrowth of anaerobes responsible for the symptoms associated with bacterial vaginosis. Other organisms that can cause bacterial vaginosis include *Atopobium vaginae, Megasphaera phylotype* 1 and 2, *Leptotrichia aminionii, Mobiluncus spp.*, *Prevotella spp.*, *Mycoplasma hominis*, *Bacteroides*

Lauren Webb is an assistant professor in the PA program at Lipscomb University in Nashville, Tenn. The author has disclosed no potential conflicts of interest, financial or otherwise.

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Key points

- Bacterial vaginosis is one of the most common causes of vaginitis symptoms.
- Traditional treatments include oral or vaginal antibiotics.
- Recurrence is common even after patients complete the entire recommended course of antibiotics, resulting in frequent antibiotic use and decreased quality of life.
- Recent studies show that vaginal or oral lactobacillus supplementation may help prevent recurrent cases of bacterial vaginosis.

spp., and bacterial vaginosis-associated bacteria (BVAB) 1, 2, and 3.[1]

Although bacterial vaginosis may self-resolve in up to 30% of cases, most women must be treated with antibiotics either orally or vaginally for symptom resolution. Although antibiotics are considered first-line therapy, 20% to 30% of women have a recurrence of symptoms after the first round of treatment.[3]

Risk factors for acquiring bacterial vaginosis include multiple or new sexual partners, intercourse without the use of condoms, smoking, use of an intrauterine device, regular vaginal douching, recent antibiotic use, having sex with another woman, and Black or Hispanic ethnicity.[1,3,4] Symptoms, if present, often include a fishy vaginal odor, abnormal vaginal discharge, and vaginal irritation.[5] Diagnosis can be performed using clinical criteria, known as Nugent score and Amsel criteria, or with laboratory tests via vaginal smear or Gram stain, with Gram stain being the gold standard.[1] Amsel criteria consider a positive diagnosis of bacterial vaginosis if the patient has three out of the four criteria:

- presence of homogenous, thin, grayish-white vaginal discharge
- positive whiff test with the application of 10% potassium hydroxide to the sample
- vaginal pH greater than 4.5
- presence of clue cells using wet-mount microscopy.[1]

Nugent scoring is less useful in clinical practice because it requires a Gram stain.[1] In clinical settings where microscopy is not available, tests such as the Affirm VP III can be used to detect *G. vaginalis*, although its presence alone does not always indicate infection.[1] The typical treatment guidelines recommend using oral or vaginal antibiotics such as metronidazole, clindamycin, or tinidazole.[5]

Although treatments under current guidelines typically lead to temporary improvement of symptoms, bacterial vaginosis has been shown to recur in at least 50% of patients within 12 months.[1] Both of the first-line antibiotics also have a high frequency of adverse reactions that may lead to reduced patient adherence with therapy. The most common adverse reactions to metronidazole include headache, vaginitis, and nausea, and the drug carries a black-box warning that it may be carcinogenic. Additionally, metronidazole may pose a risk of cumulative neurotoxicity, as well as adverse reactions to its use in the first trimester of pregnancy or with alcohol.[6]

The most common adverse reactions to oral clindamycin include pseudomembranous colitis, nausea, vomiting, and diarrhea, because this antibiotic destroys the normal flora of the gastrointestinal (GI) tract, and if given intravaginally may cause worsening vaginitis.[7] Bacterial vaginosis also is associated with complications such as preterm delivery, pelvic inflammatory disease, and increased acquisition of sexually transmitted diseases including HIV.[4] Therefore, clinicians should offer patients preventive options to avoid these potential negative consequences of bacterial vaginosis. Also, no universal standards exist for treating recurrent bacterial vaginosis, and it should be managed more aggressively to help prevent frequent use of antibiotics and potential complications in these patients.

Studies have shown that several probiotics, including oral *Lactobacillus acidophilus*, intravaginal *L. acidophilus*, *L. rhamnosus* GR-1, and *L. fermentum* RC-14, can increase the number of vaginal lactobacilli and return the vaginal microbiome to normal.[2] Oral probiotics ascend to the vaginal tract after excretion from the GI tract with bowel movements. Therefore, oral probiotics also may be effective for vaginal replacement of probiotics.[2] Because probiotics can return the vaginal flora to normal, they may not only be helpful for preventing recurrent bacterial vaginosis but also may help treat it.[2] However, most studies use the traditional antibiotic treatment of 500 mg of oral metronidazole twice daily for 7 days, with either concurrent probiotic therapy or the use of probiotics after treatment to prophylactically prevent bacterial vaginosis recurrence.[8] Although research findings on probiotics for the prevention of recurrent bacterial vaginosis generally show statistically significant improvement rates with no known adverse reactions, the route, specific probiotic, and dosing vary greatly.

LITERATURE REVIEW

A literature search was performed using PubMed, Science Direct, and Cochrane database with search terms including *bacterial vaginosis, prevention,* and *probiotics*. Initially, this search resulted in 117 articles. The search was then narrowed with filters for *clinical trials* and *within last 10 years*. Fifteen articles addressing bacterial vaginosis and probiotics were found, some focusing on prevention with probiotics and some on adding adjunctive probiotics to the initial antibiotic treatment. Eight of those articles addressed the prevention of recurrent bacterial vaginosis with probiotics, and only four of those were within the last 5 years. These studies, which use inconsistent treatment protocols, are summarized in **Table 1**.

One treatment protocol that reduced the rate of recurrent bacterial vaginosis started with oral metronidazole 500 mg

TABLE 1. Probiotic treatment regimens for recurrent bacterial vaginosis

	Bohbot and colleagues[8]	Russo and colleagues[5]	Vicariotto and colleagues[9]	Homayouni and colleagues[2]
Probiotic	*L. crispatus*	*L. acidophilus* GLA-14 and *Lactobacillus rhamnosus* HN001 in combination with bovine lactoferrin	*L. fermentum* LF15 and *L. plantarum* LP01 with the addition of 50 mg of tara gum	*L. acidophilus, Lactobacillus rhamnosus* GR-1, and *L. fermentum* RC-14
Route	Intravaginal	Intravaginal	Intravaginal	Oral
Timing	Started after failed traditional antibiotic treatment	Started concurrently with traditional antibiotic treatment	At time of diagnosis of bacterial vaginosis	No specific timing requirements
Treatment duration	Daily for 14 days	Daily for 7 days. After this, for maintenance for the next 6 months, 2 capsules taken for 10 days at the start of each menstrual cycle.	Daily for 7 nights, followed by 1 tablet every 3 days for the following 3, for a total of 4 weeks of treatment	Daily for 60 days

twice daily for 7 days. After completing the metronidazole and clinical resolution of symptoms based on Amsel criteria, patients were started on vaginal capsules of *L. crispatus* daily for 14 days. The probiotic was continued through four menstrual cycles. This study resulted in 41% (16 of 39) in the placebo group with at least one recurrence and 21% (8 of 39) in the probiotic *L. crispatus* group, indicating an effective reduction in recurrence with the use of vaginal lactobacillus ($P = .0497$).[8]

Other studies that have found probiotics useful for bacterial vaginosis have started patients on oral metronidazole and vaginal probiotic therapy concurrently. One study used *L. acidophilus* GLA-14 and *L. rhamnosus* HN001 in combination with bovine lactoferrin in women with recurrent bacterial vaginosis, in addition to traditional therapy with metronidazole.[5] The treatment group was given probiotic and metronidazole therapy together on day 1 of treatment and both were taken for 7 days. For maintenance therapy and prevention of bacterial vaginosis, patients were advised to take two probiotic capsules daily for 10 consecutive days each month for 6 months, starting the first day of the menstrual cycle.[5] Because menstrual blood increases the vaginal pH, women may become more susceptible to developing bacterial vaginosis during menstruation, which is the reason for the timing of therapy in this study. Nugent score ($P < .05$) and recurrence rates ($P < .05$) were improved in the probiotic group compared with the placebo group.[5]

One study used slow-release vaginal tablets of 400 million live cells per dose of *L. fermentum* LF15 and *L. plantarum* LP01 with the addition of 50 mg of tara gum, which has been shown to prevent adherence of *Gardnerella* bacteria.[9] Each participant was advised to use the vaginal tablet once daily for 7 nights, followed by one tablet every 3 days for the following 3 weeks, for a total of 4 weeks of treatment. The next month, they were advised to use one tablet per week in an attempt to prevent a recurrence.[9] This treatment course statistically resulted in less recurrence in the lactobacillus group after treatment ($P < .001$) compared with the placebo group, with the use of an unpaired *t*-test.[9]

As previously mentioned, oral lactobacilli have also been shown to help restore normal vaginal flora.[2] Although oral probiotics are unlikely to be as effective as vaginal preparations because they are not directly applied to the affected area, they may be a helpful option for patients who wish to avoid the vaginal preparation. One study showed that use of more than 10^8 colony-forming units of oral lactobacillus daily for 2 months can assist in curing existing bacterial vaginosis and preventing its recurrence.[2] The study also confirmed that long-term treatment with lactobacillus can prevent relapse after conventional therapy with metronidazole.[2] Other benefits of oral probiotics include prevention of bowel disease, improvement of overall immune health, improvement of hypercholesterolemia and hypertension, and improvement of postmenopausal symptoms.[10]

DISCUSSION

In women of reproductive age, bacterial vaginosis is the most common vaginal infection and occurs in up to 70% of women.[3] Probiotics have been shown in multiple studies over many years to be effective at restoring the normal vaginal flora and improving rates and symptoms of bacterial vaginosis. However, probiotics are not often used or recommended in these patients in the clinical setting. Recurrent bacterial vaginosis may lead to frequent antibiotic use, potential antibiotic resistance, loss of time at work or school, and significant interpersonal concerns. Although it is not a sexually transmitted infection (STI), bacterial vaginosis also can increase the patient's likelihood of acquiring STIs such as HIV and human papillomavirus, pelvic inflammatory disease, and preterm labor.[3] Patients with bacterial vaginosis are at an increased risk of acquiring infections due to a release of enzymes that reduce the effectiveness of host leukocytes.[3]

Based on the recent research on the prevention of recurrent bacterial vaginosis with probiotics, lactobacillus supplementation may be appropriate for select patients with bacterial vaginosis. Probiotics could be started concurrently with antibiotic treatment, or after completion of antibiotics, and continued for several weeks to prophylactically treat and prevent a recurrence. However, studies

are limited and small, with a large variety in treatment protocols. Also, no probiotics are FDA-approved for preventing bacterial vaginosis. More research is needed to determine the optimal dosing and strain of probiotic for preventing recurrent bacterial vaginosis.

CONCLUSION

Bacterial vaginosis is one of the most common causes of vaginitis symptoms.[1] Traditional treatment options include oral or vaginal antibiotics, but recurrence is common even after patients complete the entire recommended course of antibiotics. This leads to reduced quality of life and increased risk of spreading or acquiring other infections.[1] These factors, in addition to concerns with the overuse of antibiotics and potential adverse reactions to antibiotic use, lead to the need for preventive options and improved guidelines on treating recurrent infections. Recent studies show that vaginal or oral lactobacillus supplementation may help prevent these recurrent infections, giving hope to those who suffer from this condition. **JAAPA**

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