A Scoping Review: Comparison of Treatment Outcomes for Bacterial Vaginosis

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Abstract

A healthy vaginal tract has a pH of 3.8-5 (Lin et al., 2021), which creates the ideal environment for microorganisms to maintain a homeostatic environment in the vaginal tract. Thus, an imbalanced vaginal pH produces conditions like yeast and bacteria to thrive. This paper utilizes scientific research articles to demonstrate using probiotics to maintain the homeostasis balance of endogenous flora in the vaginal tract when diagnosed with bacterial vaginosis. Antibiotics can disrupt the delicate balance of the vagina's endogenous flora.

Keywords: Lactobacillus, biofilm, bacterial vaginosis (BV), probiotics, antibiotics, the potential of hydrogen (pH), endogenous flora, estrogen, ecosystem, microorganisms, microbiome, microbiota, epithelium, colony forming units (CFUs), *Gardnerella vaginalis,* glycogen

Introduction

What smells fishy and has a grey, white discharge? Bacterial vaginosis (BV) is an imbalance of the known anaerobic bacteria named *Gardnerella vaginalis* (Abou Chacra et al., 2022). BV is the most common cause of vaginal discharge. Approximately 30% of childbearing women have been diagnosed with this condition (Abou Chacra et al., 2022). The discharge smells fishy and presents with a greyish-white discharge (Abou Chacra et al., 2022).

Standard mainstay drug treatment options for BV include systemic antibiotics such as metronidazole, clindamycin, tinidazole, and secnidazole (Abou Chacra et al., 2022). The ingredients in metronidazole antibiotics are extremely harmful to use in the body, causing more damage than good. They include corn starch, magnesium stearate, gelatin, black iron oxide, titanium dioxide, FD&C Green No. 3, and D&C Yellow No. 10 (Pfizer, 2023). The antibiotic ingredients harm the host due to the synthetically manufactured composition derived from petrochemicals (Khalid et al., 2023; Oreko & Samuel, 2022). Shekhar & Petersen (2020) study found the following:

> Antibiotics induce microbiota perturbations or dysbiosis, which alters the host's immune responses against pathogens (p. 2).

Thus, in turn, creating an environment more susceptible to mutations of bacteria (Patangia et al., 2022). Antibiotics kill all the microbiome, whereas pre/probiotic promotes the endogenous flora biofilm (Patangia et al., 2022).

Background

The pH balance of the vaginal microbiome is incredibly delicate. Antibiotics, due to their inability to decipher between good and bad bacteria, can leave the vaginal microbiome incredibly vulnerable. Antibiotics kill all bacteria leaving the host more susceptible to other infections like

yeast and chronic recurrent BV infections (Patangia et al., 2022). Whereas research indicates, pre/probiotics can stabilize the ph. The purpose of this scoping review is to identify the appropriate treatment of BV, considering whether pre/probiotics are helpful or antibiotics such as metronidazole. BV indicates a wet prep with a vaginal microbiology report, which shows a positive whiff test with a fishy odor, elevated pH, and clue cells (Kairys & Garg, 2017). BV has an overgrowth of the anaerobic bacterium *Gardnerella vaginalis* (Kairys & Garg, 2017). Antibiotic treatment options for BV included metronidazole, *five-hundred* micrograms *twice* daily for *seven* days.

The *population* focus is on females of childbearing age (15-44) who are sexually active with a diagnosis of bacterial vaginosis. The *intervention* is treatment options with metronidazole versus pre/probiotic therapy. The *comparison* is metronidazole antibiotic treatment to re-establish the pH imbalance in the vaginal microbiome in contrast to pre/probiotic therapy. The *outcome* pre/probiotics are just as effective, if not better, at treating bacterial vaginosis in childbearing females prone to BV. The *time* is a seven-day treatment course. The research question translates into:

PICO-T: *In biological females of childbearing age (15-44) who are sexually active with a diagnosis of bacterial vaginosis, does a treatment of seven days with metronidazole provide a similar outcome versus seven days treatment with pre/probiotic to restabilize the vaginal normal pH levels?*

Search Methods

The literature search was obtained using the University of North Dakota School of Medicine and Health Science (SMHS) Library webpage. CINDAHL Ultimate was the primary source for the literature search for the content contained ELSEVIER and BMC Women's Health

published articles. A second literature search used for ease was PubMed. These databases are used based on scientific references with scholarly explanatory research on probiotics for treating BV.

Keywords in CINDAHL Ultimate search criteria were *bacterial vaginosis or vaginal discharge, or vagina ph*. Inclusion criteria *are pre/probiotic use, original articles, journals, and research studies/findings comparing antibiotics use versus probiotics in treating bacterial vaginosis*. Exclusion criteria *outdated* articles over the last five years, and systematic review. This search resulted in *one hundred one* results. Ten citations were found during this search. The inclusion criteria are anything published within the years *twenty-nineteen* to *twenty-twenty-three.* Rationale supports the PICO question in research with probiotics to prevent BV. The other remaining articles were not prevalent in this review.

The second search using PubMed keywords in the search engine was *Probiotics and vaginal microecology.* There were *three thousand three hundred seventy* findings. Inclusion criteria were articles published within the *years twenty nineteen* to *twenty-twenty three*. The exclusion criteria were *outdated* articles. *One hundred* articles were reviewed. *Five* citations were found helpful in this review. Concluding the list for the scoping review incorporated *fifteen* articles. The rationale for the *five* articles supports the review of microecological imbalances in the vaginal biofilm and the use of probiotics in restabilizing the endogenous flora balance.

Results

The search findings included meta-analysis, peer-reviewed journals, manuscripts, Manufacturer's recommendations, literature reviews, and systematic reviews. The strength of the research studies is rated by levels A, B, C, D, E, and MA.

Kunze & Larsen's (2019) BV literature-review level of evidence E suggests the biofilm in the elevated pH imbalance is dominated by *Gardnerella vaginalis.* Thus, it creates the perfect environment for BV to thrive (Kunze & Larsen, 2019). The literature review implies that a healthy vaginal tract with *lactobacillus* dominant will have a healthy pH and normal microbiota (Kunze & Larsen, 2019). Suggesting daily consumption of *lactobacillus* probiotics will increase the healthy pH with more lactobacillus and decrease the amount of *Gardnerella vaginalis* (Kunze & Larsen, 2019).

Women who have an increased sugar intake/diet, vaginal douching, multiple male or female sex partners, women in a long-term committed monogamous relationship with a male partner, long term use of birth control have a higher risk of BV, decreased estrogen, and smoking (Kunze & Larsen, 2019; Jones, 2019). Women with a higher risk of BV are those susceptible to alterations in the women's biofilm, which alters the normal *epithelium* microbiome or pH of the vaginal tract (Kunze & Larsen, 2019). Another research study by Joseph et al. (2021) on multiple case study levels of research E suggests the importance of *estrogen* is when there are decreased amounts make not as much of *glycogen*, in turn creating insufficient amounts *of lactobacilli* to maintain a healthy vaginal pH and restrain harmful bacteria away. Over-more the perfect opportunity for BV-causing bacteria to overgrow (Kunze & Larsen, 2019)

Nurainiwati et al. (2022) peer-review and meta-analysis level of evidence A and E findings support the PICO-T question with *a ninety* percent recovery rate in women with BV after probiotic administration, implying probiotics enhance vaginal homeostasis. Vodstrcil et al. (2021) level of evidence D manuscript findings support the PICO-T question by encouraging *lactobacillus* to dominate the state in the vaginal canal and follow-up decreased recurrence rates

when *lactobacillus* is dominant. Thus antibiotics change the genital microbiomes of both women with BV and their partners.

Recurrence after antibiotic treatment with metronidazole for women positive with BV is fifty to eighty percent three months following an overgrowth or infection with BV (Nurainiwati et al., 2022; Vodstrcil et al., 2021). Faught & Reyes (2019) integrative review level of evidence C findings support probiotics to treat BV. However, further research is needed to change the mainstay antibiotic treatment options due to limitations with many reoccurrence rates. The many limitations women experience recurrence with BV; thus, the bacteria are persistent, leaving a residual infection, becoming resistant to current antibiotic treatment options, and reinfection by a current infected partner, either male or female. Women with persistence of BV may arise to the creation of a biofilm protecting *Gardnerella vaginalis* from antibiotic therapy, thus encapsulating the *Gardnerella vaginalis*, making the antibiotics impossible to penetrate (Faught & Reyes, 2019). Lastly, poor adherence to treatment creates resistance to antibiotic therapy (Faught & Reyes, 2019). Probiotics, prebiotics, and botanical treatments have shown effective treatment of BV (Faught & Reyes, 2019). Therefore, education is crucial to the prevention of BV recurrence and resistance. In comparison, antibiotics are the mainstay for treatment of BV. The literature review suggests that prebiotics and probiotics are healthy and effective alternatives to treating BV (Wang et al., 2019).

CFUs are colony-forming units. Pre/probiotics are crucial in providing health benefits when administered in necessary amounts to the body/host (Spacova et al., 2020). Prebiotic foods include but are not limited to garlic, onions, leeks, asparagus, chicory root, agave, and cocoa (Kehinde et al., 2020). Probiotics are found in certain foods, such as Greek yogurt, kefir, kombucha, and sauerkraut (Asaithambi et al., 2021). Frequently with the Americanized diet of

processed foods and preservatives, women cannot consume the recommended pre/probiotics during the day, increasing the BV bacteria to thrive. This is the benefit of having a capsule of the probiotic for daily intake in preventing BV or treating a current BV infection. Li et al. (2017) supports the PICO-T question through the systematic review and meta-analysis with the level of evidence A and C by adding blinded randomized control trials comparing the treatment using probiotic verse the antibiotic metronidazole. The findings imply that compared to antibiotic therapy, probiotics-only therapy results in beneficial outcomes for cure rates in the clinical setting (Li et al., 2017). Probiotics regimes are safe, with *one billion* CFUs of *Lactobacilli*-based suggesting short- and long-term benefits to help treat and cure BV with a *seven* days dose (Li et al., 2017).

The literature review by Elsharkawy et al. (2018) on a double-blinded randomized controlled study level A for research findings indicates that the use of continuous vaginal probiotics shows equal effectiveness to short repetitive courses of antibiotics with similar cure rates and prevention of relapse, which supports the PICO-T question. The meta-analysis literature search article on probiotic use effective treatment for BV indicates that probiotics are equally sufficient, if not more than metronidazole, in establishing a healthy vaginal endogenous flora. Wang et al. (2019) meta-analysis findings:

> Involved 10 Randomized controlled trials with a low or moderate risk of bias, which. Suggested that the treatment with probiotics alone was more effective in the therapy of BV in the short- and long-term; however, probiotics used after antibiotic treatment were effective only for the short term (p. 10).

The suggested treatment for BV is a pre/probiotic by Nuven Naturals named *gut health* that sufficiently treats BV once per day, preferably with a meal for *seven days*. The *seven-day*

treatment option with pre/probiotics can stabilize the microbiome, with the CFU prompting a homeostatic environment. Pre/probiotic treatment alone showed a reliable benefit in effectiveness for BV oral treatment over antibiotics like metronidazole (Wang et al., 2019). *Lactobacilli*, the main ingredient in the pre/probiotics, produces H2O2 and lactic acid, which suggests inhibiting BV-associated bacteria growth (Wang et al., 2019). Wang et al. (2019) meta-analysis review implies that primary-line oral antibiotics with metronidazole are avoidable by contrast with the successful treatment with probiotics-only therapy suggesting the recurrence rate will drop significantly. There are some limitations to using pre/probiotics, such as ethnic-specific efficacy and the data on the microbial population within the vaginal microbiomes (Wang et al., 2019). Probiotics are inexpensive, around *thirty* dollars for a month's supply, and can eliminate the need for recurrent BV infections and multiple rounds of harmful antibiotics, thus being a cheaper treatment option.

Implications for Practice

Women can buy pre/probiotics over the counter or consume a diet rich in pre/probiotic foods to prompt healthy endogenous flora vaginal biofilm. Their risk of BV decreases due to the host being in a homeostatic environment. However, there are still risks for altering the vaginal pH, such as semen, vaginal douching, and lubricants; the vaginal microbiome is designed to be able to maintain the pH balance after these have altered the pH when consuming the right foods and taken a probiotic if consumption is limited. The woman can also decide whether they would like to try an oral antibiotic like metronidazole with a probiotic. Otherwise, opt for the probiotics alone to treat the BV, as the literature review has suggested to be sufficient, if not better, in treating BV. The literature review suggests that women can successfully treat BV using probiotics and not risk wiping the entire vaginal endogenous flora, maintaining and stabilizing

the pH (Wang et al., 2019). The literature review implies that treatment with a *seven-day* course of probiotics once daily with a meal is equally effective, if not more, than traditional oral antibiotics like metronidazole in preventing recurrence and treating BV. When l*actobacillus* dominates the vaginal tract, this balance inhibits the overgrowth of *Gardnerella vaginalis*, which decreases the woman's susceptibility to acquiring BV (Kunze & Larsen, 2019). In turn, this implies that taking a probiotic is equally effective, if not more than antibiotics like metronidazole to treat BV (Li et al., 2017; Wang et al., 2019; Kunze & Larsen, 2019; Elsharkawy et al., 2021; Vodstrcil et al., 2021; Nurainiwati et al., 2022; Abou Chakra et al., 2022).

Conclusion

Having a fishy-smelling vagina can be frustrating and embarrassing. However, there are solutions to this problem. Luckily pre/probiotics with *lactobacillus* can re-establish the pH balance within the vaginal tract eliminating the overgrowth of *Gardnerella vaginalis* causing BV fishy smell and odor. Antibiotics do not decipher from good or bad bacteria, whereas pre/probiotics promote a healthy balance of bacteria. Thus, causing increased recurrence rates with antibiotic use and needing multiple rounds of antibiotics to "treat" the BV. This scoping review implies that a *seven-day* course *of* pre/probiotics is a safe and effective treatment for BV preventing recurrence when taken to establish a healthy pH with *lactobacillus* dominant vaginal normal microbiota. However, pre/probiotics like antibiotics have limitations due to the nature of the microbiota.

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Appendix

PICO-T QUESTION: *In biological females of childbearing age (15-44) who are sexually active with a diagnosis of bacterial vaginosis, does a treatment of seven days with metronidazole provide a similar outcome versus seven days of treatment with pre/probiotic in the goal of restabilizing the vaginal normal pH levels?*

Literature Review Table for Synthesis

Source	Purpose/Thesis	Type of Article/ Theory/Research/etc.	Level of Evidence	Major Findings	Findings 1
Wang, Yining, & Zheng (2019)	Assess the effectiveness of probiotics for the treatment of bacterial vaginosis	Meta-Analysis	A	95% effective with combined treatment	Long-term benefits for BV treatment
Nurainiwati et al. (2022)	Probiotics to maintain biofilm and endogenous flora, gut-brain axis	Peer-review; meta-analysis	A, E	90% recovery rate in women with BV after probiotic administration; Probiotics enhance vaginal homeostasis	Probiotics suggest treatment is effective for BV
Abou Chacra, L., Fenollar, F., & Diop, K. (2022)	Pathophysiology of Bacterial Vaginosis and the different microbiomes	Peer-review	E	Different strains of bacteria found within the normal pH flora of the vaginal tract, the primary cause of BV	Lactobacillus main probiotic to reduce bacterial microbiota

Pfizer, 2023	Active ingredients in metronidazole	Manufacturer's recommendation	MA	Petrochemical ingredients	Ingredients: corn starch, magnesium stearate, gelatin, black iron oxide, titanium dioxide, FD&C Green No. 3, and D&C Yellow No. 10
Khalid et al., 2023	Petrochemicals	Manufacturer's recommendation	MA	Petrochemical ingredients (petroleum-based ingredients)	
Oreko & Samuel, 2022	Petrochemicals	Manufacturer's recommendation	MA	Petrochemical ingredients (petroleum-based ingredients)	
Shekhar & Petersen (2020)	Impacts of antibiotics on the host, consequences host health	Peer-review	D	Antibiotics induce microbiota perturbations or dysbiosis, which alters the host's immune responses against pathogens (p. 2).	Negative impacts of oral antibiotics on the body alter the host normal; endogenous flora.
Patangia et al., 2022	Negative impacts of antibiotics on the body/host	Integrative review	B	Antibiotics kill all the microbiome, whereas pre/probiotic promotes the normal flora, endogenous biofilm.	

Kairys & Garg, 2017	Gardnerella vaginalis (GV) bacterium with overgrowth in the vaginal tract	Meta-Synthesis of qualitative studies	A	Epidemiology of Gardnerella Infection	Growth of BV bacteria-causing agent, enhancing effective care with antibiotics.
Kunze & Larsen, 2019	GV bacterium implicated with the development of BV in the vaginal tract	Literature Review	E	Biofilm and virulence, dysbiosis, lactobacillus, elevated pH imbalance, and lactobacillus dominate the vaginal tract in a healthy pH. In contrast, BV has increased GV and fewer lactobacillus species, suggesting that daily lactobacillus probiotics will increase the healthy pH with more lactobacillus and diminish GV.	
Jones, 2019	BV review recurrence, treatment options	Peer-Review	D	Recurrence rate, immunocompromised, preterm birth, postpartum vaginal infections, decreased estrogen.	

Joseph et al., 2021	Vaginal microbiome review, how to prevent the occurrence of BV	Multiple case reports	E	advanced molecular tools to monitor and evaluate the extent of dysbiosis within the vaginal microbiome, particularly how specific microbial population changes compared to a healthy state. Moreover, treatment failure and BV recurrence rates remain high despite the standard antibiotic treatment. Consequently, researchers have been probing into alternative or adjunct treatments, including probiotics or even vaginal microbiota transplants, to ensure successful treatment outcomes and reduce the colonization by pathogenic microbes of the female reproductive tract.	

Vodstrcil et al., 2021	A robust body of evidence supports the exchange of bacteria between partners during sexual activity. While the hypothesis that women treated for BV are subsequently reinfected with BVAB following sex with an untreated sexual partner is not new, failure of past partner treatment trials has eroded confidence in this concept.	Manuscript	D	Encourage a lactobacillus dominant state in the vaginal canal; assess how antimicrobials change the genital microbiomes of women with BV and their partners to ensure the most effective regimens are utilized.	
Faught & Reyes, 2019	Antibiotics effective treatment options for BV	Integrative Review	C	Antibiotics remain the mainstream for treating BV, even with the high reoccurrence rates; Initial studies on biofilm disruption, probiotics and prebiotics, and botanical treatments have shown some promise but must be studied further before use in the clinic. Despite limitations, antimicrobial therapy will remain the	

				mainstay of treatment for recurrent BV for the foreseeable future.	
Spacova et al., 2020	Career development outcomes of probiotics effective to health outcomes in the host	Peer-reviewed professional organizational standards	D	Pre/probiotics are pivotal in human and animal physiology by influencing digestion, immune development, vitamin production, and likely behavior and mental well-being.	
Kehinde et al., 2020	Identifies different probiotic and prebiotic foods	Peer-review	D	sauerkraut, yogurt, kombucha, fermented foods	
Asaithambi et al., 2021	Identifies different probiotic and prebiotic foods	peer-review	D	Agave, inulin	

Li et al., 2017	The effect of probiotic therapy on bacterial vaginosis (BV) is controversial. We conducted a meta-analysis of the efficacy and safety associated with probiotic treatment for BV. Methods: We searched multiple databases covering up to 1 March 2018. Studies published as blinded randomized controlled trials (RCTs) comparing treatment using probiotic versus active or placebo control in BV patients were included, with at least one-month follow-up. Random effects model and trial sequential analysis (TSA) were applied. Results: Ten studies (n = 2321) were	Systematic-review; meta-analysis	A, C	Probiotic regimes are safe and may exhibit short-term and long-term benefits for BV treatment. The ethnic-specific result for the probiotic after antibiotics is worthy of further study.	

	included. Compared with the placebo, the probiotics-only therapy resulted in a beneficial outcome both in clinical cure rate at the 30th day (risk ratio, RR = 2.57; 95% confidential interval, 95% CI: 1.96 to 3.37) and Nugent score (mean difference, MD = −2.71; 95% CI: −3.41 to −2.00). This effect decreased but remained significant after eight weeks. Probiotics-post-antibiotics therapy had a decreased effect only for the short term and possibly among studies with a primarily black study population. No extra adverse events were observed. The TSA suggested a				

	larger sample size for practical evaluation of the probiotics as a supplementary remedy.				

Elsharkawy et al., 2021	Treatment with antibiotics and probiotics	Randomized control study	A	After initial treatment of bacterial vaginosis with vaginal clindamycin cream, the continuous use of vaginal probiotics is equally effective to short repetitive courses regarding cure rates and relapse prevention.	