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Review

Bacterial vaginosis: Literature review of treatment options with specific emphasis on non-antibiotic treatment

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Bacterial vaginosis (BV) is a vaginal infection that occurs when the balance of bacteria in the vagina is altered. It is a common condition affecting millions of women. Although the syndrome is curable with standard drugs such as metronidazole and clindamycin, relapse rates are high. Many patients are asymptomatic and recurrence is difficult to differentiate from treatment failure. The infection can have gynaecological and obstetric complications. In addition, there is an association with the transmission of sexually transmitted infections (STIs) including HIV/AIDS. This review focuses on the epidemiology, aetiology, diagnosis, complications and treatment of BV, with emphasis on the role of non-antimicrobial treatment options. Firstly, the lowering of the vaginal pH is discussed as one possible treatment option. An overview is given of the use of acetic and lactic acid gels, boric acid suppositories, as well as studies that reported on the use of douches and tampons. Thereafter, the role of *Lactobacillus* (probiotic) supplementation as treatment is discussed. Literature sources recommend that more research on BV be conducted. Although standard pharmacological therapy is effective, there are limited treatment options available. Recent research indicating the presence of a structured polymicrobial *Gardnerella vaginalis* biofilm attached to the endometrium may have major implications for future research into the pathogenesis and treatment of BV.

Key words: Bacterial vaginosis (BV), vaginal pH, acidic vaginal gel, *Lactobacilli, Gardnerella vaginalis,* anaerobes, non-antibiotic treatment.

INTRODUCTION

Bacterial vaginosis (BV) is a vaginal infection that occurs when the equilibrium of the natural flora in the vagina is altered. It is the most common cause of abnormal vaginal discharge (Wilson et al., 2005; Donders, 2010), affecting millions of women of reproductive age annually. Although the syndrome is curable with antimicrobials such as metronidazole and clindamycin, relapse rates are high.

BV may be asymptomatic (Donders, 2010) but is more commonly associated with vulvovaginal symptoms such as discharge, itch, odour and discomfort. These are common complaints of women, occurring most commonly during and shortly after menstruation, at a time when the vaginal pH tends to be elevated compared with other times in the menstrual cycle (Melvin et al., 2008). The reason for the rise in pH is unclear, but there is evidence of a temporary disturbance of the vaginal microflora and an increased incidence of BV and candidal infection around the time of menstruation (Melvin et al., 2008; Eschenbach et al., 2000). There is also increasing evidence that the pathogenic effects of BV are not confined to the lower genital tract(Swidsinski et al., 2013) and that the microbial correlate of BV involves a dense, highly structured

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polymicrobial biofilm, primarily consisting of *Gardnerella vaginalis*, strongly adhering to the vaginal epithelium (Swidsinski et al., 2005).

The primary aim was to review non-antibiotic treatment options for bacterial vaginosis. The article focuses on the epidemiology, aetiology, diagnosis, complications and non-antibiotic treatment options. A controlled literature review was conducted from January, 2012 to June, 2013 on available non-antibiotic treatment options for BV and their effectiveness. Electronic databases (for example, PubMed, EBSCOhost and ScienceDirect) were interrogated with combinations of the following key words: bacterial vaginosis, BV, abnormal vaginal flora, vaginal pH, acidic vaginal gel, *lactobacilli*, anaerobes and vaginal infection.

NORMAL VAGINAL FLORA

The vaginal flora of women without BV is typically made up of Gram-positive rods, with a predominance of *Lactobacillus crispalus, Lactobacillus jensenii* and *Lactobacillus iners* (albeit the *L. iners* is often not found as it does not grow readily on Rugosa agar) (Johnson et al., 1985). Some studies have shown that vaginal microbial composition is dependent on factors such as geographical area, for example, the normal vaginal flora in African women is considered as pathogenic for women in other regions (Berza et al., 2013). In addition, the most common lactobacillus in India is considered *Lactobacillus reuteri*, but in Finland it is *L. crispatus* (Berza et al., 2013). There is also a change in bacterial flora during the various periods of the menstrual cycle (Eschenbach et al., 2000) but the overall numerical bacterial population appears stable (Johnson et al., 1985). The various species that have been found in the normal vaginal flora have been described by Johnson et al. (1985).

EPIDEMIOLOGY OF BACTERIAL VAGINOSIS

BV is the most common vaginal infection among women in their reproductive years (Donders, 2010; Morris et al., 2001). BV is also the most common cause of vaginal discharge and malodour (Mania-Pramanik et al., 2009). Generally, it is estimated that 1 in 3 women will develop the condition at some point in their lives. Its prevalence ranges between 4.9 and 36% in developed countries (Henn et al., 2005). An increased risk for the development of BV has been shown with surgery and pregnancy where it is estimated that 15 to 20% of pregnant women have BV (Alfonsi et al., 2004). Other studies have reported the prevalence of BV among non-pregnant women to range from 15 to 30%, and have reported that up to 50% of pregnant women have been found to have BV (Laxmi et al., 2012). In a recent study by Nelson et al. (2013) among urban, primarily African-American pregnant women, 74% were identified with Nugent score BV.

The prevalence of BV varies around the world. Kenyon et al. (2013) conducted a systematic review on the global epidemiology of BV. The BV prevalences were found to vary considerably between ethnic groups in North America, South America, Europe, the Middle East and Asia. Although BV prevalence is, in general, highest in parts of Africa and lowest in much of Asia and Europe, some populations in Africa have very low BV prevalences and some in Asia and Europe have high rates. If these findings are considered, it can be concluded that RTI has a varying degree of prevalence rate among people of different communities which might be due to various factors such as socio-demographic characteristics, sexual practices and hygiene behaviour.

BV is often linked to sexual behaviour, and the epidemiological profile of BV mirrors that of established sexually transmitted infections (STIs) (Verstraelen et al., 2010). There is, however, not conclusive evidence whether BV pathogenesis involves sexual transmission of pathogenic micro-organisms from men to women. *Gardnerella vaginalis* carriage and BV occurs rarely with children, but has been observed among adolescents (even sexually non-experienced girls), contradicting that sexual transmission is a necessary prerequisite to disease acquisition (Verstraelen et al., 2010). Although male-to-female transmission cannot be ruled out, there is little evidence that BV acts as an STD. BV is therefore rather considered as a sexually enhanced disease (SED), with frequency of intercourse being a critical factor (Verstraelen et al., 2010).

AETIOLOGY OF BACTERIAL VAGINOSIS

The aetiology of BV is poorly understood and remains a subject for debate. BV can arise and remit spontaneously or develop into a chronic or recurrent disease (Donders, 2010). There are no proven individual predisposing factors exclusive to BV (Henn et al., 2005). Risk factors that have been associated with BV include having multiple sex partners, a new male sex partner, sex with a woman, early age at first intercourse, frequent vaginal douching, use of vaginal foreign bodies or perfumed soaps, cigarette smoking and lack of vaginal *Lactobacilli* (Cherpes et al., 2008). Although BV has never been proven to be sexually transmitted, it has an epidemiological profile consistent with that of a sexually transmitted infection (STI) (Henn et al., 2005), although it is better described as a SED. It is more common among women who have an STI or who use intrauterine devices (Fethers et al., 2008; Wilson et al., 2007). Women who have never had sexual intercourse may also be affected.

BV may sometimes affect women after menopause. The decrease in oestrogen levels in perimenopausal and postmenopausal women has been linked to an abnormal vaginal flora of 35 and 70%, respectively when compared

to the normal flora (Wilson et al., 2007). It has also been shown that amenorrhoea lowers the risk of BV as the absence of blood maintains vaginal pH, low and stable around pH 4.5. Subclinical iron deficiency (anaemia) is a strong predictor of BV in pregnant women (Verstraelen et al., 2005), especially in developing countries. A longitudinal study published in 2006 showed a link between psychosocial stress and BV independent of other risk factors (Verstraelen et al., 2005).

It is generally acknowledged that vaginal *Lactobacilli* play an essential role in maintaining an environment that limits the growth of pathogenic microorganisms in the vagina (Mania-Pramanik et al., 2009). It has been suggested that the presence of oestrogen and *Lactobacillus* are needed to achieve an optimal vaginal pH of 4.0 to 4.5 (Melvin et al., 2008; Suresh et al., 2009). After puberty under the influence of oestrogen, glycogen is deposited in the vaginal epithelial cells, which is metabolised by vaginal epithelial cells to glucose (Suresh et al., 2009). *Lactobacilli* produce lactic acid from glucose, keeping the vagina at an acidic pH (Suresh et al., 2009). Some species of *Lactobacilli* produce hydrogen peroxide which is toxic to various microorganisms (Suresh et al., 2009). Bacterial vaginosis is therefore characterized by an alteration of the normal acidic *Lactobacilli*-predominant vaginal ecosystem to a vaginal milieu dominated by mixed anaerobic bacteria flora (Table 1) with an accompanying increase in pH (Geva et al., 2006).

The complex aetiology of BV of a continuum of changes in the vaginal flora, rather than a single pathogen infection (Morris et al., 2001), includes a $\log_{10}$-fold increase in the numbers of facultative anaerobes listed in Table 1 (Srinivasan et al., 2008) and a concurrent loss of indigenous *Lactobacillus*-predominant vaginal microflora. The development of a more anaerobic environment inhibits the growth of *Lactobacilli*. Srinivasan and Fredricks (2008) give a complete overview on the vaginal flora in BV from a microbiological and molecular perspective.

It is unknown whether the loss of *Lactobacilli* precedes the BV infection or is a result of the infection (Mania-Pramanik et al., 2009). Furthermore, it is not known whether the change in flora is not the result of an as yet unidentified aetiological factor, suggesting that the altered flora is actually a downstream event of BV (Nansel et al., 2006). The overgrowth by the facultative anaerobes is associated with an increase in protease production especially carboxypeptidase which leads to the breakdown of peptides to amines which in an environment of higher pH can become volatile. Due to the flexible nature of the disease process, the host response in BV should be considered, although most work has been performed on the changes in micro-bial flora. It was initially believed that inflammation is absent during BV (Morris et al., 2001) but it has since been shown that median levels of IL-1β, TNF-α, IL-6 and Il-8 in intermediate stages (between normal flora and BV) and BV are similar but significantly higher than in normal flora (Hedges et al., 2006). A subtle but significant inverse relationship has also been noted between IL-1β and the presence of *Lactobacilli* in the vagina.

Recurrences frequently occur after treatment. Recurrent BV is generally defined as three or more proven (clinically by Amsel's criteria or microscopically) episodes of BV in 12 months (Amsel et al., 1983; Wilson, 2004; Hay 2009). It is postulated that BV recurs around the time of menstruation (Henn et al., 2005) when oestrogen levels are low and vaginal pH is higher than normal (Wilson et al., 2007). With treatment, the cure rates are 80 to 90% at one week, but recurrences are reported in 15 to 30% within three months (Wilson et al., 2005; Wilson, 2004). Women with recurrent BV appear to have a lower initial cure rate (Wilson et al., 2005). In a study of women with recurrent BV, complete clinical and microscopic cure occurred in only 23% of episodes following treatment, raised vaginal pH was present in 65%, positive amine whiff test in 15% and abnormal Gram-stained flora in 24% (Larsson, 1993). Women who developed early recurrence tended to still complain of an abnormal discharge or, if asymptomatic, continued to have significant abnormalities of vaginal flora (Cook et al., 1992).

Recent literature on BV epidemiology has largely focused on the presence of *Gardnerella vaginalis*, which is now recognised as a key pathogen in BV (Verstraelen et al., 2010). Recent research (Swidsinski et al., 2013) has also indicated that the pathogenic effects of BV are not confined to the lower genital tract. BV is strongly associated with late foetal loss (Oakeshott et al., 2002) and preterm birth (Leitich and Kiss, 2007), possibly due to an ascending genital tract infection pathway, though the precise mechanisms are not clear. Substantially higher rates of BV have been documented in infertile patients (Wilson et al., 2002). According to Salah et al. (2013) BV is strongly implicated in female infertility and is probably an underestimated cause of unexplained infertility.

An increased risk of early pregnancy loss associated with BV has also been found (Ralph et al., 1999). The microbiological correlate of BV has been shown to involve a dense, highly structured polymicrobial biofilm, primarily consisting of *G. vaginalis*, strongly adhering to the vaginal epithelium (Swidsinski et al., 2005). This may explain the recurrent nature of this condition (Swidsinski et al., 2008), since this has also been shown for other biofilm-associated infections.

DIAGNOSIS OF BACTERIAL VAGINOSIS

At least 50% of women with BV have no symptoms (Henn et al., 2005) and there is a debate on whether this form of BV should be considered a disease (Nansel et al.,

Table 1. Major species of bacteria found in a healthy vagina as compared to one with bacterial vaginosis.

Normal flora	Abnormal flora
Predominantly Gram Positive Rods	*Gardnerella vaginalis*
Lactobacillus crispalus	*Mobiluncus* species
Lactobacillus jensenii	*Prevotella* species
Lactobacillus iners	*Mycoplasma hominus*
-	*Atopobium vaginae*
-	*Bacteriodes* species
-	*Peptosteptococcus* species
-	*Porphyromonas* species

Source: Donders (2010) and Srinivasan et al. (2008).

2006). In the other half, BV most often manifests clinically as a thin homogenous vaginal discharge, a pH of more than 4.5, presence of “clue cells” and an amine odour (after addition of 10% of KOH). Few or no *Lactobacilli* are usually found through microscopy in the vaginal fluid (Larsson, 1992). Several methods are currently in use for the diagnosis of BV (Cook et al., 1992). Amsel criteria (Table 2) have been used in most studies as the gold standard.

Clue cells are vaginal squamous epithelial cells with coccobacilli-shaped bacteria densely adhered to them and obscuring their borders and making these appear indistinct rather than clearly defined (Khan et al., 2007). Furthermore, there is a significant lack of polymorphonuclear lymphocytes characterised by < 1 PMN per squamous epithelial cell. The sensitivity and specificity of > 20% clue cells in the diagnosis of BV is 81 and 99%, respectively and clue cells are said to be the single most reliable predictor of BV (Henn et al., 2005). Other methods rely only on microscopically confirmed criteria of a Gram-stained smear. The Nugent scoring system classifies vaginal smears into normal flora, intermediate flora or BV infection according to the number of bacterial morphotypes counted per field of vision. In this scale, a score of 0 to 10 is generated. This method is time consuming and requires trained staff, but it has high inter-observer reliability. The scores are as follows (Nugent et al., 1992):

1. 0 to 3 is considered negative for BV.
2. 4 to 6 is considered intermediate.
3. 7+ is considered indicative of BV.

A simpler scoring system applied to Gram-stained smears is described by Hay and Ison whereby only the correlation between the different morphotypes is examined, rather than the exact number per field of vision (Hay et al., 1994):

1. Grade 1 (Normal): *Lactobacillus* morphotypes predominate.
2. Grade 2 (Intermediate): Mixed flora with some *Lactobacilli* present, but *Gardnerella* or *Mobiluncus* morphotypes also present.
3. Grade 3 (Bacterial Vaginosis): Predominantly *Gardnerella* and/or *Mobiluncus* morphotypes. Few or absent *Lactobacilli*.

What this technique loses in inter-observer reliability, it makes up in ease and speed of use. Each method has advantages and drawbacks. The Amsel criteria have subjective components (macroscopic judgement of the vaginal discharge and reliance on examiner olfaction) and require access to a microscope. The Nugent and Hay/Ison methods both require a microscope and specially trained staff for Gram-staining and bacteria counts. Vaginal pH testing alone is highly sensitive, but it is not specific for BV (Henn et al., 2005; Charonis et al., 2006; Thulkar et al., 2010). Various commercial tests to diagnose BV are in use (Henn et al., 2005). Molecular techniques have been used to characterise the normal and BV associated flora but to date are not used in routine diagnosis (Donders, 2010).

COMPLICATIONS OF BACTERIAL VAGINOSIS

More important than symptoms are complications associated with BV. These appear to be related to an increased risk of susceptibility to STIs including infection with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, HSV-1 and -2, and an increased risk of HIV acquisition, and to an adverse outcome of pregnancy (Geva et al., 2006). BV has been shown to increase the risk of gynaecological and obstetric complications such as preterm labour and delivery, chorioamnionitis, post-caesarean endometritis, post-abortion pelvic inflammatory disease and cervicitis. Several groups had found that bacterial vaginal flora has an impact on these complications (Johnson et al., 1985), while other studies disproved some of these findings. The leading hypothesis concerning these associations is that absence of protective *Lactobacilli* increases biological susceptibility of acquiring an STI upon exposure (Alfonsi et al., 2004). However, the

Table 2. Amsel criteria for diagnosis of bacterial vaginosis.

No.	Criteria
1	Typical vaginal discharge (adherent, homogenous, milky or creamy coating the vaginal wall)
2	Raised vaginal pH>4.5
3	Positive “whiff amine test” (amine odour with addition of 10% KOH to the discharge)
4	Presence of >20% clue cells found through microscopy in the vaginal fluid

Three of the following criteria must be present for a diagnosis of BV. Source: Amsel et al. (1983), Henn et al. (2005), Alfonsi et al. (2004), Cook et al. (1992) and Khan et al. (2007).

temporal nature of the association between BV and acquisition of STIs remains an ongoing discussion. Although there is evidence favouring the plausibility that BV also incurs an elevated risk for HPV acquisition (Khan et al., 2007), this also remains a matter of debate. Since the 1970’s BV has been associated with pelvic inflammatory disease in the absence of *Chlamydia* or *Neisseria gonorrhea* (Morris et al., 2001). Finally, there is also a potential link between BV and an increased risk of HIV infection (Mania-Pramanik et al., 2009).

A Cochrane study (McDonald et al., 2011) found that the administration of antibiotics during pregnancy for overgrowth of abnormal bacteria in the birth canal does not reduce the risk of babies being preterm. A more recent Cochrane review confirmed this finding that antibiotic treatment can eradicate bacterial vaginosis in pregnancy, but that the overall risk of preterm birth was not significantly reduced (Brockhurst et al., 2013). Furthermore, it has been shown that BV increases the risk of miscarriage between 13 and 24 weeks (Donders, 2010), the risk of babies being preterm and a 40% elevated risk of low birth weight (Morris et al., 2001).

STANDARD PHARMACOLOGICAL TREATMENT OF BACTERIAL VAGINOSIS

Bacterial vaginosis is usually only treated if symptoms are present. Standard treatment guidelines on the treatment of BV are available, such as the “Sexually transmitted diseases treatment guidelines, 2010” (Workowski et al., 2010) and a Cochrane review entitled "Antibiotics for treating bacterial vaginosis in pregnancy" (Brocklehurst et al., 2013).

Poor results in the treatment of BV have been found with sulfonamide creams, erythromycin and tetracyclines as well as iodine gels. Ampicillin has a slightly better cure rate (66%), but the most successful treatment is metronidazole applied as a vaginal gel which has a higher than 90% cure rate in one week (Morris et al., 2001). Standard treatments of BV with antibiotics are described as unpleasant, may induce bacterial resistance with repeated use, and are associated with a high relapse rate beyond one month after the completion of treatment (Johnson et al., 1985).

NON-ANTIBIOTIC TREATMENT OPTIONS FOR BACTERIAL VAGINOSIS

Various studies have looked at non-antibiotic treatment options for BV if standard antimicrobial treatment is not available. These studies can be grouped into two categories, namely:

1. Lowering the vaginal pH; and
2. Treatment with *Lactobacilli*.

ROLE OF PH IN THE TREATMENT OF BACTERIAL VAGINOSIS

Lactobacillus-dominant flora is associated with a vaginal pH in the range of 3.6 to 4.5 (normal vaginal pH in women of reproductive age). As raised vaginal pH facilitates the proliferation of the colonising BV-associated bacteria (Alfonsie et al., 2004; Cherpes et al., 2008), one therapeutic option in the management of recurrent BV is therefore to keep the vaginal pH at 4.5 or less, in order to prevent overgrowth of bacteria until the normal *Lactobacilli* are re-established. The different methods that have been or are used to lower vaginal pH are shown in Table 3.

ROLE OF PROBIOTICS IN THE TREATMENT OF BACTERIAL VAGINOSIS

Treatment of BV using recommended antibiotics is often associated with failure and high rates of recurrence. This led to the concept of replacing the depleted *Lactobacilli* using probiotic strains as a treatment approach (Senok et al., 2009). If a decrease in the population of *Lactobacilli* appears to be the first event leading to BV and relapses are often associated with failure to restore a healthy, *Lactobacillus*-dominant vaginal flora, then the administration of *Lactobacilli* might contribute to the treatment of BV (Morris et al., 2001). For decades, some women have used L. acidophilus in yogurt or supplements to treat BV. Two RCTs investigating the efficacy of Lactobacillus species for recurrent BV were conducted. The first RCT was a cross-over study comparing the ingestion of

Table 3. Methods currently in use or being investigated to lower vaginal pH.

Treatment	Application	Results
Lactic acid	Gel tampons	Randomised Controlled Trial (RCT) with 42 women with recurrent BV. Treated with lactic acid gel rather than antibiotics to clear BV. After 6 months with 3 treatments per month, 88% vs 10% (treatment vs placebo, p<0.001) showed clinical improvement with *lactobacilli* re-establishing.
Acetic acid	Gel douche	RCT with 61 women with recurring BV. First treated with antibiotics and if BV not cleared treated with acetic acid gel. Reduced the recurrence of BV from 4.4 episodes per year to 0.6 episodes per year.RCT with 44 patients with acetic acid gel being applied twice daily for 7 days did not show conclusive results in reducing BV.
Acid buffering gels	Gel	Not as effective as metronidazole gels and discontinued.
Boric acid	Douche	Has theoretical promise of lowering vaginal pH. The acidic environment is supposed to get rid of abnormal flora and exclude yeasts. An RCT through the University of British Columbia in order to expand women's options in treating BV.
Lemon/lime	Douche	Has theoretical promise in lowering vaginal pH.Used extensively in especially West Africa. No data to support efficacy against BV.

Source: Andersch et al. (1990), Simoes et al. (2006), Holley at al. (2004), Van der Wijgert et al. (2001) and Hemmerling et al. (2007).

yoghurt containing live *L. acidophilus* with pasteurised yoghurt in 46 women with recurrent BV, recurrent candidiasis or both (Hemmerling et al., 2007). Among women with recurrent BV, episodes of BV were signi-ficantly reduced in those ingesting live yoghurt (from 60% at the start of treatment to 25% after 1 month) compared with those ingesting pasteurised yoghurt (from 60 to 50%; p = 0.004). However, these results must be interpreted with caution because the dropout rate was high and only seven women completed the entire treatment protocol.

Drago et al. (2007) investigated the effect of a *L. acidophilus*-strain-based douche in restoring a normal vaginal flora. They conducted an open-label pilot evaluation of 40 women with BV. The Nugent score decreased significantly from BV or an intermediate flora toward a normal flora during treatment, and remained low during the follow-up period for almost all of the patients, indicating BV in 52.5 and in 7.5% of the patients before treatment and at follow-up, respectively. After treatment, significant decreases in vaginal pH were observed, and the odour test became negative in all the patients. The study concluded that the treatment of BV with a vaginal douche containing a strain of *L. acidophilus* contributed to the restoration of a normal vaginal environment (Shalev et al., 1996).

Another RCT compared the use of vaginal capsules containing a mixture of *L. gasseri* and *L. rhamnosus* with placebo vaginal capsules (Larsson et al., 2008). After initial treatment with clindamycin 2% intravaginal cream, 100 women with BV were randomised to receive vaginal gelatine capsules containing either freeze-dried *Lactobacilli* or identical placebo. At the end of the study, 65% of the *Lactobacilli*-treated women had no recurrence of BV, compared with 46% of the placebo-treated women. The difference between the groups in time from cure to relapse was statistically significant (p = 0.027) in favour of the *Lactobacilli* treatment.

A further study (Shalev et al., 1996) investigated the effectiveness of vaginal administration of *L. rhamnosus* after conventional metronidazole therapy. However, randomisation in this study was not blinded, and there was no comparator arm. Some experts claim that dairy *Lactobacillus* is not the strain that normally lives in the vagina. This is why dairy *Lactobacillus* does not work for the treatment of BV. But researchers have found that two different types of *Lactobacillus* - *L. crispatus* and *L. jensenii* are most commonly found in a healthy vaginal environment. Research is now focusing on using these types of *Lactobacilli* in capsules (Boskey et al., 1999).

A Cochrane review (Senok et al., 2009) investigating the evidence for the use of probiotic preparations either alone or in conjunction with antibiotics for the treatment of BV did not find probiotics useful. Current research does not provide conclusive evidence that probiotics are superior to or enhance the effectiveness of antibiotics in the treatment of BV. In addition, there is insufficient evidence to recommend the use of probiotics either before, during or after antibiotic treatment as a means of ensuring successful treatment or reduce recurrence (Marcone et al., 2008; Andreeva et al., 2002; Milani et al., 2003). Larger, well-designed randomized controlled trials with standardized methodologies are needed to confirm the benefits of probiotics in the treatment of BV.

CONCLUSION

A number of studies have been published on the treatment of BV, and although the standard treatment with antibiotics is effective, most studies on non-antibiotic therapies are inconclusive. Some studies showed positive results for vaginal

acidification to normalise bacterial flora, while others could not prove that it is an effective method for the treatment of BV. Also, the use of probiotics, especially *Lactobacillus* showed some positive results but the studies are mostly inconclusive. In addi-tion, given that BV can also be asymptomatic, recurrence can often not be differentiated from treatment failure. Recent research indicating the presence of a structured polymicrobial *Gardnerella vaginalis* biofilm attached to the endometrium may have major implications for the further understanding of the pathogenesis of BV and the adverse pregnancy outcomes in association with bacterial vaginosis. Most literature sources recommend that more research be conducted into BV, since although standard pharmacological therapy is effective, antimi-crobial resistance may become a problem; there are limited available treatment options and relapse rates remain high.

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