BACTERIAL VAGINOSIS – AN OVERVIEW OF CHANGE IN VAGINAL MICROBIOME, ASSOCIATED CO-MORBIDITIES AND TREATMENT MODALITIES

1Shalley Dahiya, 2Raminder Sandhu, 3Bijender Singh, 4Surinder Kumar

1Medical Officer, Department of Microbiology, BPS GMC for Women, Khanpur Kalan, Sonepat, Haryana, India.

2Assistant Professor, Department of Microbiology, BPS GMC for Women, Khanpur Kalan, Sonepat, Haryana, India.

3Medical Officer, General Hospital, Bahadurgarh, Haryana, India.

4Professor, Department of Microbiology, BPS GMC for Women, Khanpur Kalan, Sonepat, Haryana, India.

ABSTRACT

Bacterial vaginosis remains the most common cause of vaginal discharge with fishy odour due to production of amines by the anaerobic bacteria. The vagina is a microbiologic battleground as different bacterial species try to gain dominance and ensure their survival due to change in external influences which effect their microenvironment. Both microbiologic and biochemical studies have outlined the remarkably complex pathophysiologic events that occur in bacterial vaginosis. The condition occurs when desirable vaginal lactobacilli are reduced in number and replaced with anaerobic bacteria which results in reduced levels of hydrogen peroxide and organic acids that usually afford tremendous advantage to maintain the healthy environment of vagina. Several major morbidities accompany this condition, including enhanced susceptibility to other sexually transmitted infections, major post operative infection and adverse pregnancy outcomes. Several antimicrobial agents have been used for treatment of symptomatic bacterial vaginosis but therapeutic success remains inadequate due to lack of clear understanding of etiopathogenesis. The objective of the current review is to highlight the complex changes occurring in vaginal microbiota responsible for bacterial
vaginosis along with currently available therapeutic options, recommendations and emerging therapies.

KEYWORDS: Bacterial vaginosis, etiopathogenesis, lactobacilli.

INTRODUCTION
Bacterial vaginosis (BV) is a common cause of malodorous vaginal discharge in women of reproductive age. Awareness of BV is low among women and they often self-medicate with antifungal agents before presentation when symptoms have become intolerable. However, many affected women are asymptomatic.[1] The condition is characterised by a thin homogeneous white discharge, a vaginal pH of greater than 4.5, a positive amine test, and the presence of clue cells microscopically. There is a change in vaginal flora from the normal lactobacilli (LB) dominant to flora with greatly reduced numbers of LB and an overgrowth of Gardnerella vaginalis, Mycoplasma hominis, and anaerobic bacteria such as Peptostreptococci, Prevotella spp, and Mobiluncus spp. There is no universally accepted definition of recurrent bacterial vaginosis, but in the few publications on the topic the definition used is three or more proved (clinically by Amsel’s criteria or microscopically) episodes of BV in 12 months.[2,3] BV was first described in 1955 by Gardner and Dukes who reported a strong correlation between BV and the presence of Gardnerella vaginalis.[4] However, progress in defining the composition of the vaginal microbiome had to await the development of new molecular techniques. These implicated not one bacterial species but numerous bacteria in BV and increased our understanding of the characteristic shift in the normal vaginal microbiota from a predominance of protective lactobacilli to pathogenic anaerobic bacteria.[5] The resident Lactobacillus species are replaced by an overgrowth of vaginal anaerobes or Gram-negative bacteria including Gardnerella vaginalis, Atopobium vaginae, bacterial vaginosis-associated bacteria, Megasphaera species, Mycoplasma hominis, Mobiluncus species, Ureaplasma urealyticum, Prevotella, and Peptostreptococcus species.[6]

VAGINAL MICROBIOTA: SHIFT IN BACTERIAL VAGINOSIS
Gram stains of vaginal fluid smears from women without BV typically show Gram-positive rods, with cultures revealing a predominance of lactobacilli, particularly Lactobacillus crispatus and Lactobacillus jensenii.[7] Lactobacilli are believed to promote a healthy ecosystem by producing lactic acid, hydrogen peroxide, and bacteriocins that have antimicrobial properties thereby excluding pathogens from this niche.[8] Gram stains of vaginal fluid from women with BV show loss of Gram-positive rods and their replacement...
with Gram-negative and Gram-variable cocci and rods.\textsuperscript{[9]} Cultures of vaginal fluid from subjects with BV typically yield \textit{Gardnerella vaginalis} and a mixture of other bacteria that may include \textit{Prevotella}, \textit{Porphyromonas}, \textit{Mobiluncus}, and \textit{Mycoplasma} species. It is not known whether the primary event which initiates BV is the loss of key lactobacilli or acquisition of the complex bacterial communities found in this syndrome; these may be simultaneous processes. It is also possible that some other factor is the primary etiological agent, and that the changes in vaginal microbiota reflect a downstream event in the pathogenesis of BV. BV is the most common cause of vaginal discharge and a frequent reason for women to seek medical attention.\textsuperscript{[10]}

\textbf{INTERPLAY OF COMPLEX FACTORS IN ETIOPATHOGENESIS}

Bacterial vaginosis is the most prevalent cause of vaginal discharge or malodour, occurring in up to 30 percent of women.\textsuperscript{[11]} It occurs when the normal \textit{Lactobacillus} species in the vagina are replaced with anaerobic bacteria resulting in reduced levels of hydrogen peroxide and organic acids usually present in the vagina. The underlying cause of bacterial vaginosis is not fully understood. More than 50 percent of women with bacterial vaginosis are asymptomatic. The fishy odour caused by production of amines from anaerobic bacteria found in many of these patients is predictive of bacterial vaginosis.\textsuperscript{[12]} When vaginal alkalinity increases after sexual intercourse (with the presence of semen) and during menses (with the presence of blood), the odour becomes more prevalent. Vaginal discharge is a more common but less specific symptom. Bacterial vaginosis is not associated with vaginal mucosal inflammation and rarely causes vulvar itch.\textsuperscript{[13]} Several factors are known to increase the risk of BV, including younger age, black ethnicity, douching, smoking, and the IUD as contraception.\textsuperscript{[14]} The link with sexual behaviour suggests that BV is sexually transmitted and that further episodes are due to re-infection. Yet, treatment of the sexual partner demonstrates no benefit in terms of recurrence rates in women. Five out of six trials, using oral metronidazole, tinidazole, or clindamycin to treat the male partner showed no benefit for the women.\textsuperscript{[15]} These findings do not support the theory of sexual transmission and reinfection. The exact mechanism for the onset of BV remains a mystery. It is associated with a reduction in lactobacilli (LB) and hydrogen peroxide production, a rise in the vaginal pH, and the overgrowth of BV associated organisms. But which of these happens first, and which is the most important? If the answers would have been known to these questions, this knowledge could have been be used for prevention of recurrences of BV.\textsuperscript{[14]}
i) Reduction in lactobacilli and hydrogen peroxide production

The main hydrogen peroxide producing strains of lactobacilli (LB) are *L. crispatus* and *L. jensenii*. The presence of these has been positively associated with being white, aged over 20 years, using barrier contraception, and low frequency of BV and gonorrhoea.[16] A cohort study showed that lack of LB gave a twofold risk of acquiring BV and no LB gave a fourfold risk.[17] Klebanoff et al showed in vitro that combining myeloperoxidases with hydrogen peroxide and a halide produced a potent oxidant, which was toxic to BV associated bacteria. Myeloperoxidase activity has been found in vaginal fluid and cervical mucus, and chloride is present in cervical mucus in amounts in excess of that required for this system. In vitro testing showed LB in high concentration (but compatible with the levels found in the vagina) were toxic to *G. vaginalis* and *Prevotella bivia*. This toxicity was inhibited by catalase indicating that hydrogen peroxide was the toxic agent. When the concentration of LB+ was lowered so that growth of the bacteria was not inhibited the addition of myeloperoxidase and chloride reinstated the toxicity. The toxic effect of this LB/myeloperoxidase/chloride system was rapid, with reduction in numbers of *G. vaginalis* at 15 minutes and complete loss of viability at one hour.[18]

ii) Change in pH

The low pH of the vagina is attributable to production of lactic acid by LB metabolism, and by the conversion of glycogen to lactic acid by oestrogenised vaginal epithelial cells. In vitro LB acidify their growth medium to a pH of 3.2–4.8 (that is, similar to normal vaginal pH). At that pH a steady state of equilibrium develops where the acidity becomes auto inhibitory. Anaerobes grow poorly at pH 4.5 or less; the optimum pH for *Prevotella* spp and *G. vaginalis* growth is 6–7. In vitro studies have shown that the concentrations of these bacteria increase with increasing pH, but both are susceptible to low pH.[19] McClean and McGroarty found that lactic acid and low pH had a greater inhibitory effect on *G. vaginalis* than hydrogen peroxide.[20] Low pH also appears to be important for LB adherence to the epithelial cells. In vitro testing showed that at pH of 4.4, a mean of 5.5 LB adhered per vaginal cell, compared with 1.4 at pH of 6.2.[21]

iii) Overgrowth of associated organisms

The initial work by Gardner and Dukes showed that BV can be produced by inoculating BV associated bacteria into a healthy vagina. *G. vaginalis* alone caused BV in only one of 13 women, but when vaginal secretions from women with BV were inoculated 11 of 15 women
developed BV. This suggests that the inter-relation between the different groups of bacteria is important for overgrowth. *P. bivia* and *G. vaginalis* have a symbiotic association. Growth of *G. vaginalis* is enhanced by ammonia which is produced by *P. bivia*. Amino acids are produced during *G. vaginalis* growth, which have stimulatory effect on the growth of *P. bivia*. It is therefore possible that the symbiotic relationship between these bacteria is due to the fact that by products of metabolism of one fuel the growth of the other. The exact aetiology remains elusive, although some authors have proposed a complex interaction between the numerous components of the vaginal microbial ecosystem and their human host.

iv) Formation of Biofilms

Biofilms are strongly associated with human infections and up to 65% of infections treated by physicians in the developed world have been attributed to biofilms. There is emerging new evidence that biofilms are associated with BV and it has been suggested that these may be critical in pathogenesis.

CLINICAL FEATURES

Women with BV may have a malodorous vaginal discharge or local irritation, but about half of the women with diagnosable BV have no clear symptoms. The high prevalence of BV and the lack of symptoms in a substantial fraction of affected women lead to the question whether BV should be considered a normal variant of the vaginal microbiota or a disease entity. For women affected by severe symptomatic BV as manifested by profuse vaginal discharge and less frequently by local burning or itching, there is little question that they have a disease. For women with laboratory evidence of BV but no symptoms, the disease designation seems inappropriate, though the condition may still impart increased risk of adverse health outcomes such as preterm birth. Antibiotics such as metronidazole and clindamycin are usually effective in treating BV in most subjects, leading to resolution of symptoms, though rates of relapse are high.

BACTERIAL VAGINOSIS AND ASSOCIATED COMORBIDITIES

Although BV is an important medical condition itself, it is associated with several more serious adverse outcomes including preterm birth, pelvic inflammatory disease, and acquisition of HIV infection. Bacterial vaginosis, even when asymptomatic, is associated with a high incidence of endometritis and pelvic inflammatory disease following abortion and gynaecologic procedures in the general population. Among women with
bacterial vaginosis, no overall increased risk of developing pelvic inflammatory disease has been found.\cite{33} Bacterial vaginosis is associated with late miscarriages, premature rupture of membranes, and preterm birth.\cite{34} Interest in BV has grown since it was found to associate with an increased susceptibility to sexually transmitted infections, herpes simplex viruses, human papillomavirus, and human immunodeficiency virus (HIV).\cite{35,36} Both symptomatic and asymptomatic bacterial vaginosis have been strongly linked with an increased risk of human immunodeficiency virus (HIV)-1 transmission (relative risk, 1.89; 95% CI, 1.46 to 2.43). In a prospective study of Kenyan sex workers, the absence of lactobacilli in vaginal cultures was associated with a 2.0-fold increase in HIV acquisition and a 1.7-fold greater risk of developing gonorrhea.\cite{37} Another similar study found that BV was associated with a 3.7-fold increase in HIV acquisition over a 2.5-year period.\cite{32} Further, women with HIV shed more virus into the cervico-vaginal discharge when BV is present.\cite{38} Women with BV are also more likely to acquire trichomoniasis and chlamydial cervicitis.\cite{39} A second complication of BV appears to be an enhanced risk of infection after pelvic surgery. Cuff cellulites following abdominal hysterectomy occurred 3.2 times more often in women with BV in a study of 161 women.\cite{40} and in 35% (7/20) of those with pre operative BV and 8% (4/50) (P < .1) of those without BV in another study.\cite{41}

BV prior to caesarean delivery has been associated with a 6-fold increase in postpartum endometritis,\cite{42} and a study has found that placement of a single intra vaginal dose of metronidazole prior to caesarean delivery significantly reduces the risk of post-caesarean endometritis among women with or without BV (RR 0.42; 95% CI, 0.19–0.92).\cite{43} BV probably increases risk for community-acquired PID,\cite{31,33,44} and plasma cell (chronic) endometritis\cite{45} and may be causative in some cases of abnormal uterine bleeding.\cite{46} BV has also been associated with decreased success of in vitro fertilization procedures.\cite{47}

BV has also been associated with postoperative infection and adverse pregnancy outcomes including premature rupture of membranes, premature labour and delivery, intra-amniotic infection, and low-birth-weight infants.\cite{48,49}

**LABORATORY DIAGNOSIS**

The diagnosis of BV is usually made using a series of clinical criteria collected by a clinician performing a pelvic examination, or by interpretation of vaginal fluid Gram stains. Amsel clinical criteria are usually employed for the diagnosis of BV in the clinical setting because the approach is rapid, but it does require access to a microscope.\cite{28}
At least 3 of 4 Amsel criteria must be present to establish a diagnosis of BV, including (1) elevated vaginal fluid pH > 4.5; (2) a positive “whiff test” which consists of the detection of a fishy odour upon addition of 10% potassium hydroxide to a slide containing vaginal fluid; (3) the presence of clue cells (>20%) in vaginal fluid which are shed vaginal epithelial cells coated with bacteria creating indistinct borders; (4) a homogeneous, milky vaginal discharge. An alternative method for diagnosis of BV relies on analysis of Gram stains performed on vaginal fluid smears. This approach is most commonly employed in the research setting where Gram stains are used to classify subjects but is less well suited to the clinical setting because analysis of the vaginal fluid Gram stains requires a degree of expertise that is rarely available in real time when the clinician is faced with the decision whether to treat for BV. For better or for worse, the vaginal fluid Gram stain is considered the current diagnostic gold standard as it offers greater reproducibility and objectivity when compared with the Amsel’s clinical criteria. For example, there can be variation between technicians in the evaluation of wet mounts for vaginal clue cells. Several scoring systems are used to classify vaginal smears. The method of Nugent et al. assesses the presence and relative amounts of three bacterial morphotypes, including Gram-positive rods (lactobacilli), Gram-negative and Gram variable rods (Gardnerella vaginalis, and Bacteroides species), and curved rods (Mobiluncus species). A Nugent score of 0–3 is considered normal (no BV) and is marked by the presence of Gram-positive rods, or at least no Gardnerella vaginalis or Mobiluncus morphotypes. A Nugent score of 7–10 confers the diagnosis of BV and is marked by the absence of Gram-positive rods and the presence of high concentrations of Gardnerella or Mobiluncus morphotypes. A Nugent score of 4–6 is designated intermediate flora and has Gram stain features between the two poles. Alternative scoring systems for interpretation of vaginal fluid Gram stains exist, such as that of Ison and Hay.

Cultivation-based approaches have identified Gardnerella vaginalis, anaerobic bacteria such as Prevotella, Porphyromonas, Peptostreptococcus, Mobiluncus, and Mycoplasma to be largely associated with the disturbed microbiota in subjects with BV. Cultivation-independent approaches have consistently documented the high proportion of fastidious bacteria in a variety of ecological niches and these tools have recently been applied to study the vaginal ecosystem. The most commonly employed target for molecular identification of bacteria is the small ribosomal subunit or 16S rRNA gene. The 16S rRNA gene is useful because it is present in all bacteria and has regions of sequence conservation that can be targeted with broad range PCR primers and areas of sequence heterogeneity that can be used to identify
bacteria or infer phylogenetic relationships. Once the 16S rRNA gene has been sequenced from a bacterium, the variable regions can be used for species-specific PCR either in a qualitative or quantitative manner. Quantitative PCR is especially useful for rapidly identifying bacteria when an internal probe is employed and for measuring how levels of vaginal bacteria change. Nine highly variable and therefore phylogenetically rich regions of the ∼1540 base pair 16S rRNA gene have been described and designated V1 to V9. The choice of primers targeting the conserved regions flanking the different variable regions can profoundly affect the diversity of bacterial species identified. While molecular methods have many advantages over cultivation approaches for characterizing microbial diversity, there are numerous limitations.

THERAPEUTIC OPTIONS

a. General considerations

Non-pregnant women with symptomatic disease require antibacterial therapy to relieve vaginal symptoms. Other benefits of treatment include decreasing the risk of HIV and other sexually transmitted infections and reducing infectious complications following abortion or hysterectomy. A Cochrane review of 24 randomized controlled trials (RCTs) showed that clindamycin and metronidazole are equally effective, achieving clinical cure in 91 and 92 percent of cases, respectively, after two to three weeks of treatment. Six RCTs showed topical and oral antibiotic preparations to be equally effective. One disadvantage of oral regimens is a longer duration of treatment. Intravaginal clindamycin cream is preferred in case of allergy or intolerance to metronidazole. Metronidazole in a single 2-g dose has the lowest effectiveness for treating bacterial vaginosis and is no longer recommended. Metronidazole, 500 mg twice daily for one week, is effective for treating bacterial vaginosis and trichomoniasis. Although lactobacillus probiotics are safe, there is no conclusive evidence that they are superior to or enhance the effectiveness of antibiotics in the treatment of bacterial vaginosis or prevent its recurrence.

ANTIBIOTIC THERAPY

Metronidazole

Metronidazole is a nitroimidazole antimicrobial agent used to manage protozoal infections such as trichomoniasis and anaerobic infections. Since the early 1980s, metronidazole has been used widely in the treatment of BV with good clinical results. Various preparations allowing a vaginal or oral administration and different regimens have been studied.
Clindamycin
Clindamycin is a second antimicrobial agent for the treatment of BV. This lincosamide antibiotic has various treatment preparations including vaginal (ovule and cream) and oral.\(^{[59]}\)

Tinidazole
Tinidazole is a nitroimidazole antibiotic and an antiprotozoal agent that was first reported in Europe, Asia, and Latin America for its use in BV treatment. Trials evaluating oral regimens of 1–2 g daily for 1–5 days have given favourable results.\(^{[61]}\)

Secnidazole
Secnidazole is a nitroimidazole antibiotic with a broad spectrum of activity against anaerobic microorganisms and has a longer half-life than metronidazole. Used as a single-dose oral regimen it appears effective in the treatment of amebiasis, giardiasis, trichomoniasis, and BV.\(^{[61]}\) It represents an attractive therapeutic option particularly in women whose likely compliance is doubtful.\(^{[59]}\)

COMBINATION THERAPY
Using oral or vaginal preparations of metronidazole and clindamycin, 80–90% of women will have an initial response to treatment but 15–30% will get a recurrence within 3 months.\(^{[62]}\) In women with recurrent BV the initial response rate appears to be lower.\(^{[2]}\) The heterogeneity of microorganisms involved in BV may contribute to treatment failure and high recurrence rates. Clindamycin has better activity against \(M.\) hominis, \(Mobiluncus\) spp, and \(G.vaginalis\) than metronidazole, but metronidazole has the advantage of not affecting LB. In trials comparing treatments, cure rates for metronidazole 400 mg or 500 mg twice daily for 7 days have been equivalent to clindamycin vaginal cream daily for 3–7 days, and to metronidazole vaginal gel once or twice per day for 5 days.\(^{[63]}\)

NON ANTIBIOTIC THERAPEUTIC OPTIONS
a. Probiotics
According to FDA and World Health Organization definitions, probiotics are “live microorganisms which when administered in adequate amounts confer a health benefit on the host.”\(^{[64]}\) The mechanism by which probiotics confer such a health benefit is not well understood. Several hypotheses concerning their mechanism of action have been proposed: (i) as an example, \(Lactobacillus fermentum\) RC-14 has been reported to produce a bio surfactant containing a large number of collagen-binding proteins that could inhibit pathogen
adhesion and induce a competitive exclusion of the pathogen on epithelial cells; (ii) probiotics may produce antimicrobial compounds such as hydrogen peroxide, lactic acid, or bacteriocins, which inhibit pathogen growth; (iii) probiotic therapy may cause a mucosal modulation that enhances the host immune system response.\cite{65,66,67}

Microorganisms with probiotic properties are \textit{L. rhamnosus} GR-1, \textit{L. rhamnosus} Lcr 35, \textit{L. reuteri} RC-14, and \textit{L. crispatus} CTV-05. Taken orally or vaginally these have been shown to improve vaginal flora without any side effects and are of potential clinical importance.\cite{68,69,70,71} Intestinal passage of probiotic has the advantage of interfering with the natural process by which pathogens emerge from the intestine and ascend along the perineum to the vagina.\cite{69} The newly recognized strains \textit{L. rhamnosus} L60 and \textit{L. fermentum} L23 have been considered for probiotics development due to their in vitro performance concerning bacteriocins production, adherence to epithelial cells, and co-aggregation with pathogenic bacteria.\cite{72} The second proposed use for probiotics is in preventing the recurrence of BV after an initial treatment. The hypothesis is that abnormalities of the vaginal flora often persist even in the absence of clinical symptoms after antimicrobial therapy.\cite{59}

b. Acidification of vaginal fluid

BV is characterized by the alkalinisation of vaginal fluid (vaginal pH > 4.5) prompting some authors to propose correcting the vaginal pH in order to treat BV. The results have been discordant. In two randomized double-blind clinical trials, vaginal acidification alone (5 mL acetic acid gel intravaginally twice daily for 7 days or 5 g acid-buffering formulation gel intravaginally once daily for 5 days) was an ineffective therapy for BV compared with placebo or metronidazole.\cite{73,74} However, in another randomized study, the combination of oral metronidazole 500 mg twice daily and 5 g lactic acid vaginal gel at bedtime for 7 days was found to be better than metronidazole alone at promoting lactobacilli colonization and reducing malodorous vaginal discharge. Moreover, not only was the lactic acid well tolerated but it also reduced recurrence of symptomatic BV.\cite{75}

EMERGING THERAPIES

Antibiotics and novel vaginal delivery systems

Vaginal delivery of clindamycin or metronidazole is the most common therapy in the treatment of BV, but its efficacy is not optimal. Some authors are working towards improving existing formulations or creating new dosage forms. One group in Egypt working on pluronic polymers, has developed a hydrogel that swells in aqueous environments for use as a drug
delivery system. This novel vaginal delivery system for metronidazole, improved the therapeutic efficacy compared with that achieved with conventional vaginal gel.\[76\] Elsewhere, a new dosage form, containing metronidazole, was developed based on vaginal mucoadhesive tablets realized by including bioadhesive polymers.\[77\] Similarly, new bioadhesive film formulations of clindamycin phosphate for vaginal delivery have also been developed.\[78\] The in vitro properties and antibacterial activity of these new formulations may offer an alternative to traditional dosage forms for vaginal topical administration. The success of such new dosage forms, and bio adhesive products designed to extend the residence time of the antibiotic in the vaginal cavity, will not only depend on their effectiveness but also on their potential toxicity for epithelial cells of the vaginal mucosa and for resident lactobacilli.\[59\]

**NOVEL THERAPIES**

i) **Antimicrobial agents**

Nifuratel, a furane-derivative, is an antiprotozoal and antifungal agent. It is safe, well tolerated, with no known teratogenic effects and can be used in the treatment of many infections of the genito-urinary tract.\[79\]

ii) **Antiseptics**

Essential oils from medicinal plants have strong antiseptic properties. Two recent studies have suggested the use of thymol and eugenol for BV therapy.\[80,81\] Thymol is a natural monoterpenic phenol found in oil of thyme, with an in vitro activity on *G. vaginalis* biofilms; and eugenol is a phenylpropene extracted in particular from clove oil. Both were applied via vaginal douche once daily for 7 days and resulted in a similar significant reduction in symptoms as that obtained with vaginal metronidazole.\[81\] Glycerol monolaurate, another antiseptic, is a safe monoglyceride with bactericidal properties for Gram-positive organisms. It is microbicidal for *Candida* and *G. vaginalis* in vitro and reduces both organisms without affecting vaginal lactobacilli in vivo when applied via vaginal gel.\[82\]

A recent study evaluated the efficacy of octenidine hydrochloride/ phenoxyethanol, a local antiseptic spray, applied for 7 or 14 days compared with 7 days of metronidazole vaginal tablets for BV therapy The local antiseptic spray was as effective as the standard therapy with cure rates of 58% and 71% at 7 days and 14 days, respectively, compared with 61% at 7 days with metronidazole.\[83\]
A temperature-sensitive gel containing silver nanoparticles has been developed in China and its antibacterial properties have been studied in vitro. This optimized silver nanoparticle dosage form demonstrated great potential, encouraging further development for the clinical treatment of BV.¹⁸⁴

iii) Prebiotics

Another alternative for treating BV is to induce a vaginal flora shift from a BV to a Lactobacillus-dominated flora by promoting the growth of lactobacilli. The principle behind prebiotics is to provide nutrients that stimulate the growth of lactobacilli. Oligosaccharides can selectively promote the growth of lactobacilli that in turn generate lactic acid to lower the vaginal pH and secrete antibacterial substances that inhibit the adhesion and replication of the anaerobic bacteria.¹⁸⁵ Some authors have proposed the topical application of a gel containing sucrose, a disaccharide of glucose and fructose, to treat BV. A Phase III clinical trial was conducted including women with symptomatic BV who were randomly assigned into three groups for vaginal application of sucrose (5 g), metronidazole (0.75%), and placebo gels, twice daily for 5 consecutive days. The therapeutic cure rates (according to FDA guidelines) evaluated 21–35 days after the start of treatment were 61%, 67%, and 7%, respectively, for sucrose, metronidazole, and placebo gel groups. These results suggest that sucrose has a therapeutic cure rate similar to the metronidazole gel. Interestingly, at the intermediate visit (7–10 days after the start of treatment), the therapeutic cure rate was statistically higher for the sucrose group (83%) than for the metronidazole group (71.3%) and the placebo group (0.9%).¹⁸⁶

REFERENCES


