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Diagnosis and Management of Bacterial Vaginosis and Other Types of Abnormal Vaginal Bacterial Flora: A Review

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Bacterial vaginosis (BV) is a common cause of abnormal vaginal discharge. It is characterised by an overgrowth of predominantly anaerobic organisms (*Gardnerella vaginalis, Prevotella spp., Peptostreptocci, Mobiluncus spp*.) in the vagina leading to a replacement of lactobacilli and an increase in vaginal pH. BV can arise and remit spontaneously, but often presents as a chronic or recurrent disease. BV is found most often in women of childbearing age, but may also be encountered in menopausal women, and is rather rare in children. The clinical and microscopic features and diagnosis of BV are herein reviewed, and antibiotic and non-antibiotic treatment approaches discussed.

Target Audience: Obstetricians & Gynecologists, Family Physicians

Learning Objectives: After completion of this educational activity, the participant should be better able to analyze bacterial vaginosis clinically, formulate an oral antibiotic treatment regimen for bacterial vaginosis and use vaginal treatments for bacterial vaginosis.

DEFINITION

Abnormal vaginal discharge can be caused by non-infectious causes, cervicitis, *Candida*, *Trichomonas vaginalis*, bacterial vaginosis (BV), and aerobic vaginitis (AV), and probably other, yet unresolved causes. The term abnormal vaginal flora (AVF) is used to indicate women with diminished lactobacillary morphotypes and overgrowth of pathogenic microorganisms.

BV is a common cause of abnormal vaginal discharge. It is characterized by an overgrowth of predominantly anaerobic organisms (*Gardnerella vaginalis, Prevotella spp., Peptostreptocci, Mobiluncus spp*.) in the vagina leading to a replacement of lactobacilli and an increase in vaginal pH. Typically a very scarce to absent immunological response is present in uncomplicated BV. In women with aerobic vaginitis (AV) the lactobacilli are also decreased and pH is elevated, but aerobic microflora derived from the gut, such as *Escherichia coli*, group B streptococci, and *Staphylococcus aureus,* are predominant, and often a significant local immune response is present.

Mixed infections are frequent.

ETIOLOGY AND TRANSMISSION

BV can arise and remit spontaneously, but often presents as a chronic or recurrent disease. Two theories prevail to explain the existence and recurrence of this mysterious condition: (1) lactobacilli disap-

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pear due to environmental factors such as vaginal douching, frequent pH insults due to sexual intercourse or other factors or (2) some lactobacilli are attacked by type specific viruses (bacteriophages) and are unable to recolonize the vagina, facilitating anaerobic overgrowth.

Although not fitting the diagnosis of "sexually transmitted infection (STI)," BV is strongly associated with sexual activity. Women having sex with women share similar lactobacillary types and are at increased risk for BV (1).

CLINICAL FEATURES

Prevalence

BV is found most often in women of childbearing age, but may also be encountered in menopausal women, and is rather rare in children (2–9). In Caucasian women the prevalence is 5% to 15%, in African and American blacks 45% to 55%. In Asian women the prevalence is less well studied, but in general is around 20% to 30%.

Symptoms

About half of women with BV have no symptoms. However, often women admit increased vaginal discharge and unpleasant smell when queried. Although BV is associated with infectious diseases of the upper genital tract and complications during pregnancy, uncomplicated BV does not cause other symptoms.

Physical Signs

Speculum examination reveals a watery, homogeneous, gray discharge, but in general the vagina is not inflamed (no edema, redness).

Complications

Usually BV is annoying due to the malodorous discharge, and sometimes the discharge can be voluminous. However, there is an association with posthysterectomy vaginal cuff infection (10–12), postabortion endometritis (13–17), increased risk of acquiring STI, especially genital herpes and HIV (18–26), increased risk of spontaneous miscarriage ranging from 13 to 24 gestational weeks (27–31), and preterm birth (31–46).

DIAGNOSIS

Clinical Diagnosis (Amsel)

Three of 4 clinical signs and symptoms of the following:

Homogeneous gray-white discharge.

Fishy smell (if not recognizable, use a few drops of 10% KOH).

Vaginal pH above 4.5.

Clue cells on wet mount microscopy (full blown BV: $\geq$20% clue cells, Partial BV: $>$0 and $<$20% clue cells).

Microscopic Diagnosis

Unstained

Smear of Fresh Vaginal Fluid. Although generally considered less accurate than Gram stain, the clinical diagnosis including fresh microscopy of vaginal fluid has excellent sensitivity and accuracy compared to Gram stained preparations (47–49). Furthermore, in trained hands, wet mount phase contrast microscopy has demonstrated excellent intra- and inter-observer agreement (50,51). Finally, it allows differentiation between more subtle forms of abnormal vaginal flora such as full blown BV, partial BV, AV, and mixed infections with BV (52,53). AV is a condition of abnormal vaginal flora which is completely different from BV: although both conditions have a depression of lactobacilli, low vaginal lactate (54,55), and increased pH in common, the microflora type with aerobic cocci and/or small bacilli in AV is completely different from the granular anaerobic flora in BV, and the latter typically lacks the presence of an immune response (vaginal leukocytes) and microscopic signs of impairment of the vaginal epithelium (presence of parabasal cells) that is seen in AV (56).

Smear of Rehydrated Air-Dried Vaginal Smears. Ideally fresh vaginal fluid is used in order not to miss the motility indicative of specific diagnoses like *Mobiluncus* or *Trichomonas vaginalis*. However, later rehydratation of an previously air-dried smear can also diagnose BV with high accuracy (sensitivity 96%, specificity 98%) (57).

Gram Stained

Nugent Score. The gold standard for BV diagnosis. However, it fails to account for other abnormal flora types than full blown BV like aerobic vaginitis. Specifically, the problem is with so called "intermediate

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flora," when the score is between that of normal flora (Nugent score 0–3) and overt BV (Nugent score 7–10). The significance of intermediate scores and whether they are in fact abnormal is not clear (53,58,59).

Ison Score. Ison's scoring of Gram stained specimens recognizes "partial BV," an intermediate form of abnormal flora that describes the presence of Lactobacilli and BV-like flora together. This form of "intermediate BV" is different from the "intermediate flora" in the Nugent system, as well as the Ison's grade 4 AV flora described by Donders (56). Therefore, if Gram stains are to be used instead of wet mounts, Ison's scoring system allows for a more complete characterization of the flora than does the Nugent score.

Papanicolaou (PAP) Stained

As Pap smears are taken anyway to detect cervical cell atypia, there use as a possible screening tool for microbial abnormalities such as BV has been investigated extensively. Although some authors have found reasonable accuracy compared with the clinical diagnosis (48,60–63), others find it to be an inaccurate test (64–66).

Cultures and Molecular Techniques

These have been used to characterize more specifically the actual composition of BV flora and to determine which components contribute to symptomatology or pathogenesis (67–73), but they have no place in the diagnostic arsenal of routine testing for BV.

MANAGEMENT

Patient Information

Patients should be informed that the condition is due to a lack of lactobacillary resistance for reasons that are not clear. Sexual activity has a role in appearance and severity of symptoms, as well as in the likelihood of recurrence. Still, the condition can also appear and be sustained in the absence of sexual activity.

Therapy

Antibiotics Against Anaerobes

Types and Dose of Antibiotics. At present 3 antibiotics are approved for treatment of BV: metronidazole, tinidazole, and clindamycin. Both metronidazole and clindamycin can be applied locally in the vagina or taken orally, and with similar efficacy. Recommended regimens (level A) are (in order of popularity of use) (1) oral metronidazole 500 mg twice daily for 5 days, (2) 2% vaginal clindamycin cream once daily for 7 days, (3) oral clindamycin 300 mg twice daily for 7 days, (4) metronidazole 0.75% vaginal gel once daily for 5 days, or the stat regimens, (5) 2 g of metronidazole, or (6) 2 g of tinidazole in a single dose.

In order to achieve complete treatment efficacy, cure is defined as a Nugent score 0 to 3 and all Amsel criteria negative. Roughly 58% to 88% of patients will be cured after 5 days treatment with metronidazole or clindamycin (74). Compared to placebo both medications are effective in blinded, well designed, randomized trials (metronidazole RR: 0.58 [95% CI: 0.44–0.78]) and clindamycin RR: 0.25 (95% CI: 0.16–0.37 in one trial and RR: 0.39, 95% CI: 0.22–0.68 in another) (75, level A). In head to head trials, clindamycin and metronidazole have equal efficacy, as shown in at least 6 trials comparing oral and vaginal formulations of metronidazole and clindamycin, both after 1 week (combined RR: 1.01, 95% CI: 0.69–1.46) and after 1 month(combined RR: 0.91, 95% CI: 0.70–1.18) (75, level A). Furthermore, no difference in treatment failures was seen after 1 week or 1 month when oral versus local applications where compared. However, in terms of side effects, in most studies clindamycin tended to have fewer adverse effects than oral metronidazole (RR: 0.75, 95% CI: 0.56–1.02), the latter primarily causing a disturbing metallic taste, stomach pains, and vomiting (75) (level A).

Vaginal Versus Oral Application. As bioavailability for both metronidazole and clindamycin is 50% lower after vaginal application, fewer side effects are to be expected (76). When compared to oral intake 400 mg twice a day for 7 days, the use of 500 mg metronidazole vaginally at night for 7 days was equally effective: after 4 weeks, resolution was 74% and 79% in the oral and the vaginal groups, respectively (74) (level B). Remarkably, in this study, copper IUD users responded significantly less often (58% vs. 88% in non-IUD users) and vaginal lactobacilli were better preserved after vaginal than after oral medication. In another randomized trial, twice daily 400 mg vaginal metronidazole was compared with 1 oral dose of 2 g tinidazole, showing again no difference in both treatment regimens (98% improvement vs. 79%, respectively) (77) (level B). However,

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it has to be noted that in this study the criteria of cure were less stringent, as improvement and cure were combined into one outcome variable. Also the study was not done in a blinded way (e.g., vaginal treatment with oral placebo and oral treatment with vaginal placebo). In a study of bioadhesive vaginal tablets, equal efficacy was found for 500, 250, and 100 mg tablets (78). Metronidazole was tested in a low dosage 0.75% cream and was superior to placebo: 87% versus 17% were cured after 2 to 3 weeks. As relapses occurred in 15% of those initially cured after 1 month, the total cure rate was 72% after 1 month, comparable to metronidazole in other series. In a randomized trial comparing the oral and the vaginal forms of metronidazole, 1 month cure rates were the same: 71% (79). Brandt found high cure rates of 89% and 92% with high doses of metronidazole in a double blind randomized trial comparing 2 g orally versus 1 g twice within 24 hours vaginally, but with fewer side effect with the latter (80) (level A).

A number of randomized studies addressed the efficacy of vaginal clindamycin versus oral metronidazole (81–84). Eradication rates at 1 month after vaginal clindamycin cream were 66% to 83% versus 68% to 87% for metronidazole (81,83,84). In one double-blinded study, the primary outcome was defined as "cure or improvement," and revealed good but noncomparable results for both regimens: 97% versus 83% in the vaginal clindamycin versus the oral metronidazole group (82) (level B). Also when oral metronidazole, vaginal 0.75 metronidazole vaginal cream, and 2% vaginal clindamycin cream where compared in a randomized trial, equal efficacies (respectively, 85%, 75%, 86%) and side effects were noted (85). Vaginal versus oral clindamycin also showed similar efficacy but somewhat fewer side effects (86).

Duration of Treatment. Another issue is the "duration of treatment." The classical duration of treatment is 5 days for metronidazole as well as clindamycin, whether given orally or vaginally. However, both shorter and longer durations have been evaluated. In comparing a 14 day schedule with a 7 day schedule, Scwebke and Desmond found an improved cure with 2 versus 1 week of treatment. (RR of failure: 0.49, CI: 0.6–0.93). However, this difference was not sustained at 4 weeks (87) (level A).

Other Antibiotics. Tinidazole in 1 or 2 g regimens was significantly superior to placebo in a double blind randomized trial (88). A 2 g single oral dose of tinidazole has been compared with vaginal and oral metronidazole, with conflicting results (77,89,). The addition of an intermittently applied acidifying gel did not improve the cure rate, nor the relapse rate (90). Compared to oral use of tinidazole, its vaginal application (500 mg daily) had a much higher cure rate, primarily due to a better efficacy in IUD users (91). A large study randomized patients to receive different 5 nitro-imidazole compounds (tinidazole, metronidazole, ornidazole secnidazole) in either oral or combined oral/vaginal formulation (92). None of the 5-nitro-imidazoles was superior to the other (cure rates: 57%–63%) after 1 month, but the combination of vaginal plus oral use was superior 80%–86%). Ofloxacillin and erythromycin were also tested in blinded randomized studies, which showed that these antibiotics have little to no effectiveness and should not be used to treat BV (93,94). Also newer compounds such as cefadroxil (95) and secnidazole (96,97) were tested, with comparable cure rates to metronidazole. Schwebke and Desmond showed no benefit of adding azithromycin to metronidazole to cure BV (87).

Side Effects of Antibiotic Treatment. Metronidazole is well tolerated in general, but is known for its nausea, pyrosis, stomach pains, and its typical disulfiram effect when alcohol is consumed while taking it (98). It is not known whether such general side effects also ensue when used vaginally. According to case-control and meta-analytic studies, metronidazole is not teratogenic in humans, even when used in the first trimester of pregnancy (99,100). Due to the difference in taste it creates in breastmilk, its use is in general ill-advised during lactation (101,102).

Clindamycin cream as well as metronidazole gel contain mineral oils that are known to diminish the strength of condoms (103,104). Therefore, use of barrier contraception is not considered safe during the treatment with any of these vaginal products. A rare but severe complication of oral of vaginal clindamycin use is pseudomembranous colitis (105), for which treatment with vancomycin, or metronidazole (106) is preferred.

Development of antibiotic resistance is another worrisome side effect. After 3 to 12 days of therapy, some BV-associated anaerobes, such as *Prevotella sp* (both *P. bivia* and the black-pigmented *Prevotella* species) become resistant against clindamycin (107), a phenomena that can last up to 90 days after stopping therapy (108). Although resistance against metronidazole of those anaerobes are much less common, recent reports of increasing resistance of *G. vaginalis* and *Mobiluncus*

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TABLE 1
Overview and meta-analysis of placebo-controlled randomized trials with oral or vaginal lactobacilli used to treat BV or to prevent recurrence of BV, at 1 week or 4 weeks after treatment*

Author	N	Study Design	Proportion of Patients Without BV After 1 wk	Proportion of Patients Without BV After 4 wk
Probiotic vs. placebo in treatment and incidence of BV				
Hallèn 1992 (114a)	30/30 SBV	Tablets *Lactobacillus acidophilus*/ placebo Vaginal application 6 d	16/28 vs. 0/29 $P < 0.0001$	3/28 vs. 0/29 NS
Neri 1993 (114b)	32/32 SBV	Yoghurt *L. acidophilus*/none Vaginal application 7 d	NA	28/32 vs. 2/32 $P < 0.0001$
Parent 1996 (114c)	17/15 SBV[†]	Tablets *L. acidophilus*/placebo Vaginal application 6 d	10/13 vs. 3/12 $P = 0.017$	7/8 vs. 2/9[‡] $P = 0.015$
Shalev 1996 (114d)	23/23[§] Mixed[¶]	Yoghurt *L. acidophilus*/ pasteurized Oral intake 2 mo	NA	16/21 vs. 9/19 NS
Reid 2001 (114e)	14 ABV 28 no BV	Lactobacilli GR1 + RC14/GG (placebo) Oral intake[‖] 28 d	2/11 vs. 0/3 21/22 vs. 6/6 NS	7/11 vs. 2/3 22/22 vs. 6/6 NS
Reid 2003 (114f)	16 ABV 48 no BV	Lactobacilli GR1 + RC14/ placebo Oral intake 60 days	NA NA	NA 19/25 vs. 0/23 $P < 0.0001$
Probiotic vs. placebo as adjuvant therapy after antibiotics for BV				
Larsson 2008 (114g)	100 BV	*L. gasseri* (LEB01) *L. rhamnosus* (PB01)/placebo after treatment with clindamycin	NA	36/37 vs. 31/39 $P = 0.028$
Total Meta-analysis				
Total patients with SBV		26/41 vs. 3/41 $P < 0.0001$		47/81 vs. 11/80 $P < 0.0001$
Total patients with ABV		2/11 vs. 0/3 NS		23/55 vs. 30/57 NS
Total patients with BV		28/56 vs. 3/44 $P < 0.0001$		70/136 vs. 41/137 $P = 0.0005$
Total patients without BV		21/22 vs. 6/6 NS		77/84 vs. 37/68 $P < 0.0001$

*Meta-analysis of these studies show that probiotics clearly reduce symptoms in symptomatic BV patients (SBV) but do not significantly improve the microscopic findings in asymptomatic BV.

[†]BV diagnosed as only 2 of 4 Amsel criteria positive.

[‡]No reason given for high drop out rates after 7 and 28 days (only half of patients competed the study).

[§]Of the 46 women, 18 had no infection, 20 BV, 8 BV + Candida, and 18 Candida. The results shown were for proportion patients with BV only.

[¶]Normal at inclusion, history of recurrent BV.

[‖]Probably oral intake, but not specified in the manuscript.

BV indicates bacterial vaginosis; SBV, symptomatic bacterial vaginosis; ABV, asymptomatic bacterial vaginosis; NA, not available; NS, not significant.

sp are noted, especially in cases with chronic, recurrent BV (109–112). According to some, clindamycin has a higher activity against *Atopobium vaginae* and *G. vaginalis* than metronidazole (113).

Nonantibiotic Treatments. Nonantibiotic treatments have been extensively tested, but not always in a randomized controlled fashion. Basically 2 types of treatments have been tried: acidification and application of lactobacilli. In the first line of treatment efforts, a single vaginal rinse with 20 mL of 3% H_2O_2 solution was compared with a single dose of metronidazole (114). Not only was clinical failure rate higher (RR: 1.75) in the H_2O_2 group, but some women experienced severe vaginal irritation.

Vaginally applied lactobacilli or oral lactobacilli in the form of yoghurt or tablets were compared to placebo in a number of randomized, controlled stud-

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ies, all showing superior effects to placebo after 1 to 4 weeks (Table 1, level A). In 2 studies, adjuvant therapy with lactobacilli after therapy with metronidazole of clindamycin was also shown to be superior for the prevention of recurrences in the 1 to 6 months after therapy, effects observed both for *Lactobacillus acidophilus* (115) and the combined use of *Lactobacillus rhamnosus GR-1* and *Lactobacillus reuteri RC-14* (GR-1/RC-14) (116) (see later). Studies comparing the use of lactobacilli with the "gold standard" metronidazole or clindamycin are scarce. In one randomized trial, a 5 day regimen of vaginal lactobacilli (GR-1/RC-14) was equal in effectiveness to 0.75% metronidazole vaginal gel at 1 week, and superior at 4 weeks (117). In another study of women with abnormal vaginal flora, including types other than BV, participants were randomized to receive either 12 days of lactobacilli with 0.03 mg of estriol, or 500 mg metronidazole vaginally for 6 days (118). One week after treatment the failure results were equal, but after 4 weeks metronidazole was superior, indicating that in order to obtain long-term effects, repetitive application with lactobacilli may be indicated.

Prevention of Recurrences. Women with frequent recurrences need extra attention to minimize the burden BV imposes on their quality of life. In one 16-week placebo controlled randomized trial, weekly vaginal metronidazole was compared to placebo, In the treatment group, 70% of women were symptom-free, versus only 30% in the placebo group (119). However, even with metronidazole maintenance therapy, after stopping the treatment for 12 weeks, only 35% of patients were still without recurrences, versus 20% of controls. Furthermore, patients who received vaginal metronidazole cream suffered from vulvovaginal candidiasis more often than placebo users ($P = 0.02$) (81). In order to prevent the need for antibiotics in repetitive courses, the adjuvant use of probiotics after an initial course of antibiotics has been tested in a number of randomized controlled trials. For 1 month after treatment with 1 g metronidazole per day for a week, 125 premenopausal Nigerian women with bacterial vaginosis were treated with oral *L. rhamnosus* GR-1 and *L. reuteri* RC-14 or placebo: 88% complete cure rate in the lactobacilli (LB) group, versus 40% in the placebo group ($P < 0.001$) and none of the LB treated women had BV versus 30% in the placebo group (116). Also in placebo controlled randomized trials, vaginal application of probiotics following treatment for BV or other forms of vaginitis were efficient in reducing the post treatment failure rate (115) and in preventing recurrences of BV over a 6 months period (120).

The problem is that most patients will have frequent recurrences after 3 to 12 months, whatever treatment has been used. In one study after 2 doses of 500 mg metronidazole for 5 days, recurrence rates were 58% (95% CI: 49%–66%) for full blown BV (Nugent score 7–10), and 69% (95% CI: 61%–77%) for abnormal vaginal flora (Nugent score 4–10) by 12 months (121). For this reason, both treatments of longer duration, as well as treatment supplements with local resistance enhancing factors have been tested. It looks like whatever regimen is tested, in most settings, prevention of recurrences is difficult. In one study, a classic 7 day regimen with twice daily oral metronidazole was compared with a regimen of daily intravaginal application of lactobacilli for 2 months. At 4 weeks, results were similar, and at 3 months, failures less frequent in the lactobacilli group (122). In 49 women with a mean of 4.4 recurrences of BV per year, use of acidifying gel could reduce the number of recurrences to 0.6 per year. However, the study used no controls and was not randomized (123). In another randomized study, acidifying gel was as efficient as 0.75% metronidazole gel (124).

Pregnancy

Most studies show an consistent increased risk of pregnancy complications in women with AVF or BV (32,125,126). The main risks are failed implantations after embryo transfer, increased spontaneous miscarriages, preterm rupture of the membranes, chorioamnionitis, preterm delivery, and postpartum endometritis, and are summarized and discussed in 2 nice overviews and a meta-analysis (35,42,127). In follow-up, the predominance of certain strains of lactobacilli, especially *Lactobacillus crispatus*, seems to provide long-term protection against abnormal vaginal flora, more than the presence of *Lactobacillus gasseri* and *Lactobacillus iners* (128). The latter even seems to be a destabilizing factor, increasing the risk to develop BV over time. Treatment studies of BV in pregnancy have been less consistent, leading to numerous meta-analyses, of which some claimed a reduced complication rate in subgroups of patients at high risk for preterm delivery (129,130), but most found no beneficial effect at all, especially in low risk women (129–139). In one careful, large RCT treating women with BV, metronidazole did not show any benefit in the prevention of preterm birth compared to placebo (140), while in

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2 other RCT, the use of metronidazole was even disadvantageous, causing an increased rather than a decreased risk for preterm birth (141,142). Furthermore, in at least 2 meta-analyses, metronidazole was found to increase the risk of adverse pregnancy outcome (137,139). On the other hand, although older RCTs of vaginal clindamycin showed no effect (143–146), 3 more recent RCTs showed benefit (in terms of preterm birth rates) for clindamycin either given orally or vaginally (147–149). Timing of medication—as early in pregnancy as possible, and at least before 20 gestational weeks—seems to be important (138).

Nonantibiotic therapy has also sporadically been tested for women with AVF or BV in pregnancy. In 1990, Holst et al reported a clear benefit of using acidifying cream for BV in a small group of women during pregnancy (150), but this paper was never followed by larger series. A Cochrane review of all randomized trial using probiotics indicated a clear reduction of vaginal infection after the use of oral or vaginal *L. acidophilus* containing milk products or yogurt, but data on the outcome of pregnancy were lacking (151).

Partner Notification

As BV is "sexually associated" but not "sexually transmitted" the partners should not be notified, although less frequent or condom protected sexual activity will be likely to limit the recurrences. Studies to reduce the number of recurrences by randomizing the partners to be treated with placebo or clindamycin have not shown any differences in the recurrence frequency of their partners (152). In one study, a vaccine against some "adverse types" of lactobacilli was claimed to have a protective effect in a placebo-controlled randomized trial, but the study was never confirmed (153). In recent literature, the presence of a vaginal biofilm favoring anaerobic growth is quoted as one of the possible reasons why frequent recurrences of BV occur in some women (154). In one study, metronidazole, even although effective in eradicating the symptoms of BV, was not able to abolish the biofilm in women with recurrent BV (155).

Disease Prevention

Although BV has been found to be related to numerous complications outside as well during pregnancy, prevention of such complications by screening and treatment policies is not firmly established. As discussed above, although pregnancy complications such as preterm birth and chorioamnionitis are strongly related to BV, it is not evident that any treatment of BV improves this outcome. In summary, in most studies metronidazole has not prevented adverse pregnancy effects. More recently, randomized studies using oral and/or vaginal clindamycin have shown a protective effect. Whether this is caused by its better treatment profile of *Atopobium vaginae* compared to metronidazole (113,156), or to the failure of most studies to detect separate flora disturbances, like aerobic vaginitis or partial BV (56), is still a matter of debate. Several authors advocate "screen and treat" policies for women undergoing medical abortions, or even spontaneous miscarriages, in order to prevent post abortion complications and recurrent miscarriages (157–159), but 1 randomized study failed to prove any benefit of treating BV before abortion (160). The role of probiotics herein is not well established.

Due to the lack of clear information about the origin and etiopathogenesis of BV, it is difficult to provide guidelines to prevent occurrence of the disease. Furthermore, as the efficacy of therapy for BV in pregnancy is not established, screening and treating in pregnancy is not indicated. However, as screening early in pregnancy and treatment with clindamycin were successful in most recent randomized trials, adhering to screen and treat policy may be defended in areas with a high prevalence of infection-related preterm birth, although further research is needed. As BV is clearly linked to the acquisition of other STI, such as HIV, herpes genitalis, *T. vaginalis*, and HPV infection of the cervix leading to cervical cancer, efforts to detect and treat AVF and BV could influence the sexual health of a great number of women worldwide, especially African women, who have a much higher incidence of both AVF and STI. Therefore, increased awareness and more research should lead to improvement of women's health by trying to control BV and other types of AVF. After completing the CME activity, the participant should be better able to analyze bacterial vaginosis clinically, formulate an oral antibiotic treatment regimen for bacterial vaginosis and use vaginal treatments for bacterial vaginosis.

Search Strategy

Pubmed and internet search was used to find related papers on "Bacterial vaginosis" OR "nonspecific vaginitis" OR "abnormal vaginal flora" OR "vaginal dysbiosis."

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To decrease the number of papers withdrawn and limit the search to differential topics, 3 subcategories were made: (1) diagnosis with the keywords "test" OR "diagnosis" OR "symptom" OR "PCR" OR "culture" OR "microscopy," (2) epidemiology with the key words "Risk" OR "prevalence" OR "incidence" OR "epidemiology" OR "occurrence," (3) complications with the key words "pregnancy" OR "complication" OR "Risk" OR "operative," (4) treatment with the key words "medication" OR "therapy" OR "treatment" OR "antibiotics" OR "probiotic" OR "side effect." When needed specific extra terms were introduced like "randomized," "placebo," "meta-analysis" etc. If the necessary information was not obtained in the lists, full internet search was performed, in Pubmed as well as in Cochrane, and by using Google.

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