Bacterial Vaginosis: A review ofPathogenesis, Diagnosis and Treatment

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ABSTRACT
Vaginal bacteriosis is characterized by increased vaginal discharge with fishy smell, usually white or gray in color and associated with dysuria. A link between psychosocial stress and bacterial vaginosis persistence even when other risk factors were eleminated. Epidemiologic data strongly support the sexual transmission of BV. Options remain limited, and inability to prevent the frequently, relentless symptomatic recurrences of BV and to reduce serious sequelae such as preterm delivery, remains an acknowledged but unresolved shortcoming. Treatment of bacterial vaginosis is important for several reasons. First, bacterial vaginosis affects 8% to 23% of women during their reproductive years, and is the most common etiology of vaginal symptoms that prompt women to seek medical care. Second, bacterial vaginosis has been strongly associated with numerous adverse sequelae related to the upper genital tract, especially in pregnant women, who experience a higher rate of preterm delivery and low birth weight infants in presence of bacterial vaginosis.The aim of the present study was to review pathogenesis, diagnosis and treatment of bacterial vaginosis.

Keywords: Bacterial Vaginosis ;Pathogenesis; Treatment

INTRODUCTION

Bacterial Vaginosis (BV) is defined as disequilibrium in the vaginal microflora with decline in the number of lactobacilli with increase of a number of bacteria including Gardnerellavaginalis creating a biofilm which allows other opportunistic bacteria to thrive **(1)**.Gardnerellavaginalis colonization or infection predominantly occur in womenand not associated with nongonococcal urethritis. G. vaginalis infections typically occur in women of reproductive age**(2,3)**.BV appears to occur more commonly among African American women than non-Hispanic white women.The reasons for this are not entirely clear**(4)**.

BV is associated with certain sexual behaviors, including oral sex, multiple sexual partners, sex during menses, lesbian sexual activity, anal receptive sex and failure to clean insertive sex toys **(5)**.

Observations in support of this include the following: incidence of BV increases with an increase in the number of recent and lifetime sexual partners, a new sexual partner can be related to BV, and male partners of women with BV may have urethral colonization by the same organism, but the male is asymptomatic **(6)**.

Pathogenesis of Bacterial Vaginosis:

Despite its public health importance, however, the pathogenesis of BV remains unclear, so much so that some refer to this condition not as an infection but rather as a dysbiosis, a microbial imbalance in the vaginal flora that can precipitate changes in the normal activities of the vagina **(7,8)**.Epidemiologic data strongly support the sexual transmission of BV**(9)**.

BV is characterized by a shift from a lactobacillus-predominant vaginal flora to one in which the lactobacilli dramatically decline and facultative and strict anaerobes abound **(10)**. Despite this dramatic shift, some women with BV do not experience symptoms **(11)**. There is agreement that the shift away from an optimal vaginal flora consisting of lactobacilli is the biological risk factor for associated adverse outcomes of BV**(12)**. This may also associated with of single or multiple pathogens or other factors lead to the overgrowth of BV-associated anaerobes**(9)**.

Others have hypothesized that BV is caused by a polymicrobial consortium of microorganisms **(13)**. Clue cells, sloughed epithelial cells from the microbial complex biofilm community of BV, have been shown to carry not only G. vaginalis but also a mixed array of anaerobes which vary among individuals **(14)**. This consortium of bacteria is thought to enhance the transmission of BV. Clue cells have been identified in male as well as female subjects **(15)**.

Treatment of Bacterial Vaginosis:

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Treatment of symptomatic women with BV is recommended; however, despite initial response, BV recurs or persists in a significant proportion of women **(16)**. This is probably due to the persistence of the biofilm, which has been documented by vaginal biopsy after therapy with metronidazole and moxifloxacin**(17)**. Alternative approaches to BV treatment, which target the biofilm, are needed **(18)**.
New drugs have not been forthcoming and are not likely to be available in the immediate future; hence, reliance on the optimal use of available agents has become essential as improvised often unproven regimens are implemented**(19)**.
Recommended first-line treatments include oral metronidazole 500 mg twice daily for 7 days, intra-vaginal 2% clindamycin cream once daily for 7 days, or intra-vaginal metronidazole gel once daily for 5 days. Also, single doses and short courses of metronidazole, tinidazole, and intravaginal clindamycin are less effective **(20)**. While short-term cure rates following first-line recommended regimens are equivalent and approach 80%, studies with extended follow-up show that recurrence rates in excess of 50% occur within 6–12 months **(21)**. These high rates of recurrence have led investigators to evaluate a range of alternative therapeutic approaches, including extended and suppressive antimicrobial regimens, combination first-line regimens, and adjunctive intravaginal and oral probiotic therapies **(22-24)**.
While some of these approaches appear promising and are under further evaluation, overall there has been limited progress in achieving sustained long-term cure following cessation of these regimens. This lack of success is a reflection of our poor understanding of the pathogenesis of both recurrent and incident BV **(25,26)**.
Higher baseline loads of some BV-associated bacteria have been associated with an increased risk of recurrence in one study **(27)**, and 2 studies showed that BV-associated biofilm re-accumulates following antibiotic therapy **(17,28)**. These data indicate that persistence of certain BV-associated bacteria and biofilm may be a determinant of recurrence following antimicrobials and raises the question as to whether antimicrobial resistance also plays a role. While there have been data indicating that clindamycin use can result in the emergence of clindamycin-resistant anaerobic gram-negative rods **(29)**, in a panel of 865 anaerobic species obtained from women with BV, resistance to metronidazole was rare (0.3%) **(30)**.
Despite evidence that there may be differences in antimicrobial susceptibility between the 2 first-line agents, overall BV cure rates following clindamycin and metronidazole have been equivalent **(31)**. Intriguingly, however, recent whole-metagenome sequencing studies have identified at least 4 clades of G. vaginalis **(32)**, with preliminary studies showing that 2 of these clades may be intrinsically resistant to metronidazole, providing one possible mechanism for BV persistence after treatment **(33)**.
Special considerations:
All symptomatic pregnant women should be tested for bacterial vaginosis and treated. Some specialists prefer using systemic therapy to treat possible subclinical upper genital tract infections among women at low risk for preterm delivery **(34)**. Recommended regimens during pregnancy includes metronidazole 250 mg orally three times a day for 7 days or clindamycin 300 mg orally twice a day for 7 days **(35)**.
Existing data do not support the use of topical agents during pregnancy. Evidence from three trials suggests an increase in adverse events (e.g., prematurity and neonatal infections), particularly in newborns, after use of clindamycin cream. Other studies have not demonstrated a constant association between metronidazole use during pregnancy and teratogenic or mutagenic effects in newborns **(36)**.
Because treatment of bacterial vaginosis in asymptomatic pregnant women at high risk for preterm delivery with a recommended regimen has reduced preterm delivery in three of four randomized controlled trials. The screening and treatment should be performed at the first prenatal visit**.**Women with bacterial vaginosis were treated at 19 weeks with a regimen of an initial dose of 2 g metronidazole, followed by a 2 g dose 2 days later; the regimen was repeated 4 weeks later this regimen was not effective in reducing preterm birth in any group of women **(35).**
Data are conflicting regarding whether treatment of asymptomatic pregnant women who are at low risk for preterm delivery reduces adverse outcomes of pregnancy. One trial, using oral clindamycin, demonstrated a reduction in spontaneous preterm birth; another indicated a reduction in postpartum infectious complications **(37).**
Treatment of bacterial vaginosis in asymptomatic pregnant women who are at high risk for preterm delivery might prevent adverse pregnancy outcomes. Therefore, a follow-up evaluation 1 month after completion of treatment should be considered to evaluate whether therapy was effective or not **(36).**

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Clindamycin cream or oral clindamycin is preferred in case of allergy or intolerance to metronidazole. Metronidazole gel can be considered for patients who do not tolerate systemic metronidazole, but patients allergic to oral metronidazole should not be administered metronidazole vaginally**(38).**

Conclusion:

We recommend adhering to current treatment guidelines rather than relying on unproven alternative regimens. An increasing recognition of the potential role of pathogen-rich biofilm in facilitating disease persistence results in hope for improved therapeutic success in the future.

It is important to acknowledge the likelihood that reinfection from partners may be contributing to recurrence and may obscure the benefits of new therapeutic approaches.

Finally, optimization of future BV treatment strategies may require combination approaches, such as antibiotics given along with biofilm-disrupting agents and in conjunction with partner treatment.

No conflict of interest.

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