BACTERIAL VAGINOSIS (BV) VS VULVOVAGINAL CANDIDIASIS (VVC) AND TREATMENT OPTIONS

Vaginitis is defined as any condition with symptoms of abnormal vaginal discharge, odour, irritation, burning or itching. [1] The most common causes of vaginitis, according to Professor Heather Paladine, Assistant Professor of Medicine in the Center for Family and Community Medicine Columbia University in New York are bacterial vaginosis (BV), vulvovaginal candidiasis (VVC) and trichomoniasis.

Writing in a 2018 article in American Family Physician, she comments that bacterial vaginosis is implicated in 40% to 50% of cases when a cause is identified, while vulvovaginal candidiasis accounts for 20% to 25%. [1]

Other studies state that bacterial vaginosis (BV) is the most common vaginal infection in women of reproductive age, with prevalence estimates ranging from 12 % in Australian women [1], to 29 % in North-American women [2, 3], and greater than 50 % in women in East/ Southern Africa. [4]

In the case of Vulvovaginal Candidiasis (VVC), an estimated 75% of women will have at least one episode of VVC, while 40%–45% will have two or more episodes. [6]

VVC can be classified as either uncomplicated or complicated. Approximately 10%–20% of women will experience complicated VVC, defined as recurrent when it entails four or more episodes in one year. [1]

Published studies on women's experiences of vaginitis (thrush and trichomoniasis) by Dr Jade E. Bilardi and Sandra Walker of the Central Clinical School at Monash University in Australia have highlighted that vaginal symptoms can make women extremely anxious and distressed, as well as feeling considerable shame and embarrassed. In particular, the physical symptoms of vaginal malodour and abnormal discharge commonly manifested in BV impacted heavily on their social and sexual lives. [3] [5]

This in turn can affect the ways in which women deal with and understand vaginitis, and how they seek help and self-care.

CAUSES

BV is described as a common cause of malodorous vaginal discharge in women of reproductive age.

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DIAGNOSIS	AETIOLOGY	SYMPTOMS	SIGNS	OTHER RISKS
Bacterial vaginosis (BV) **Contributing risk factors:** Low socioeconomic status, vaginal douching, smoking, new or multiple sex partners, unprotected intercourse, sex between women	Anaerobic bacteria (Prevotella, Mobiluncus, Gardnerella vaginalis, Ureaplasma, Mycoplasma)	Fishy odour; thin, homogenous discharge that may worsen after intercourse; possible presence of pelvic discomfort.	No inflammation	Increased risk of HIV, gonorrhoea, chlamydia and herpes type 2 infections
Vulvovaginal candidiasis (VVC) **Contributing risk factors:** Recent antibiotic use, pregnancy, uncontrolled diabetes mellitus, AIDS, corticosteroid use, other immunosuppression	Candida albicans; can have other Candida species	White, thick, cheesy or curdy vaginal discharge; vulvar itching, pain or burning; redness and swelling around vaginal opening; burning during urination or intercourse; no odour.	Vulvar erythema and oedema Symptoms often worsen just prior to menstruation	—

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Interest in BV has grown considerably since longitudinal studies established that it is linked to an approximate two-fold increased risk of acquiring various sexually transmitted infections (including chlamydia, gonorrhoea, herpes simplex type 2 and HIV infection).[2] [4]

While the exact aetiology of BV is still unclear, it appears to be a polymicrobial condition which is associated with a complex interaction between the numerous components of the vaginal microbial ecosystem and their human host. This results in a profound disturbance of the normal vaginal flora. [2]

Vulvovaginal Candidiasis is usually caused by C. albicans but other Candida sp. or yeasts may also occasionally cause it. [6].

DIAGNOSIS AND PRESENTATION

Paladine stresses that history alone is unreliable for the diagnosis of different causes of vaginitis, stressing that 'physical examination findings and office-based or laboratory test results should be used with the history to determine the diagnosis.' [1]

Diagnosing BV utilises clinical criteria (i.e., Amsel's Diagnostic Criteria) or a Gram stain, which is considered the gold standard laboratory method [6]. Clinical diagnosis of BV is based on the combination of any three of the following four criteria: vaginal pH > 4.5, thin homogeneous vaginal discharge, clue cells on microscopic examination of vaginal fluid and a "fishy" amine odour. [2]

VVC can be diagnosed by visualisation of yeast hyphae on potassium hydroxide preparation in patients with typical symptoms or using antigen or DNA probe testing [1]. The clinical presentation that may suggest a diagnosis of vulvovaginal candidiasis is the presence of external dysuria and vulvar pruritus, pain, swelling and redness. Signs include vulvar oedema, fissures, excoriations and thick curdy vaginal discharge. [4] [6]

Paladine stresses in her article that with complicated VVC, 'culture is particularly important for its diagnosis and treatment because patients are more likely to have an infection with nonalbicans strains of Candida, which may require different treatment.' [1]

A small percentage of women (<5%) have Recurrent Vulvovaginal Candidiasis (RVVC). The pathogenesis is poorly understood and most women with RVVC have no obvious predisposing or underlying conditions. [6]

Paladine highlights the typical clinical signs, symptoms and risk factors for Bacterial vaginosis (BV) and Vulvovaginal candidiasis (VVC) in Table 1. [1]

TREATMENT OPTIONS FOR BV AND VVC

Bacterial vaginosis

Treatment of bacterial vaginosis is recommended for resolving symptoms and reducing the risk of other infections mentioned in Table 1. First-line therapy includes five-day courses of intravaginal metronidazole (Metrogel), oral metronidazole (Flagyl) or intravaginal clindamycin, [1] according to Professor Paladine, adding that 'no significant difference in effectiveness has been demonstrated among these regimens.' [1] She also stresses the importance of considering patient preference when choosing an agent.

Possible side effects of clindamycin. [7]

- nausea
- vomiting
- diarrhea
- stomach pain
- joint pain
- vaginal itching or discharge
- skin rash or itching
- heartburn
- sore throat
- changes in bowel habits (especially in older adults).

Possible side effects metronidazole [8]

- Agitation
- back pain
- blindness
- blurred vision
- burning, numbness, tingling, or painful sensations in the hands or feet
- changes in speech patterns
- confusion
- decreased vision
- depression
- dizziness
- drowsiness
- eye pain
- fever
- headache
- irritability
- lack of coordination
- nausea
- seeing or hearing things that are not there
- seizures
- shakiness and unsteady walk
- slurred speech
- stiff neck or back
- trouble speaking
- unsteadiness, trembling, or other problems with muscle control or coordination
- unusual tiredness or weakness
- vomiting
- weakness in the arms, hands, legs, or feet

In a comprehensive article published in the International Journal of Women's Health, Jean-Pierre Menard outlines current antibacterial treatment and emerging therapies for bacterial vaginosis. [2]

METRONIDAZOLE – THE MAINSTAY OF BV TREATMENT

Metronidazole has been used widely in the treatment of BV since the early 1980s with good clinical

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results. Menard comments that 'this nitroimidazole antimicrobial agent is used to manage protozoal infections such as trichomoniasis and anaerobic infections.' [2].

Studies have been conducted on various metronidazole preparations using different regimens and a vaginal or oral administration. Menard remarks that since vaginal regimens have been associated with fewer gastrointestinal complaints (33% vs. 52%), vaginal metronidazole may be an alternative to oral metronidazole. [2]

In its most recent updated 2015 treatment guidelines for sexually transmitted diseases, the Centers for Disease Control (CDC) states that treatment of BV is recommended for women with symptoms, adding that the established benefits of therapy in non-pregnant women are to relieve vaginal symptoms and signs of infection. [6]

The CDC recommended regimens for BV are as follows:

- Metronidazole 500 mg orally twice a day for 7 days OR
- Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days OR
- Clindamycin cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days.

METRONIDAZOLE VAGINAL GEL IS A POPULAR CHOICE IN SOUTH AFRICA

Locally, one of the most commonly prescribed treatments for BV in clinical practice is the antimicrobial MetroGel V, containing the same CDC-recommended regimen of Metronidazole 0.75%. Supplied in a once-daily dosing treatment, MetroGel V is a water based, fragrance-free gel formulation which is applied intravaginally daily at bed time for five days.

MetroGel V can be used for recurrent BV as studies have shown a decreased incidence of resistance. Intravaginal metronidazole helps to restore vaginal Lactobacilli colonisation. According to clinical studies Metrogel V showed a 61 % increase in the growth of vaginal Lactobacilli one week after treatment, in comparison to treatment with clindamycin which only showed 11 % growth of Lactobacilli. [6]

Persistent and recurrent BV: The 2015 CDC guidelines note that there is limited data regarding optimal management strategies for women with persistent or recurrent BV. 'Using a different recommended treatment regimen can be considered in women who have a recurrence; however, retreatment with the same recommended regimen is an acceptable approach for treating persistent or recurrent BV after the first occurrence.' [6]

It advocates that metronidazole gel 0.75% twice weekly for 4–6 months has been shown to reduce BV recurrences in women with multiple recurrences after completion of a recommended regimen, but notes that this benefit might not persist when suppressive therapy is discontinued.

The CDC 2015 guidelines furthermore recommend treatment of BV for all symptomatic pregnant women. 'Although metronidazole crosses the placenta, no evidence of teratogenicity or mutagenic effects in infants has been found in multiple cross-sectional and cohort studies of pregnant women. Data suggest that metronidazole therapy poses low risk in pregnancy.' [2]

Menaud confirms the use of Tinidazole (a nitroimidazole antibiotic and an antiprotozoal agent) and Clindamycin (an antimicrobial agent and lincosamide antibiotic) as alternative regimens for BV. [2] [6]

Tinidazole: 2 g orally once daily for 2 days, or 1 g orally once daily for 5 days

Clindamycin: 300 mg orally twice daily for 7 days or ovules 100 mg intravaginally once at bedtime for 3 days

He also mentions Secnidazole, a nitroimidazole antibiotic with a broad spectrum of activity against anaerobic microorganisms, adding that it 'represents an attractive therapeutic option particularly in woman whose likely compliance is doubtful.' [2]

Turning to non-antibiotic therapy for BV, Menard's article highlights several other options, notably probiotics. He remarks that while two recent reviews supported the use of probiotics, [2], 'further randomised controlled trials are needed before definitive conclusions can be made on the effectiveness of probiotics for the treatment of BV.'

Another novel antimicrobial agent, according to Menard is Nifuratel, a furane-derivative. As an antiprotozoal and antifungal agent, 'it is safe, well tolerated and with no known teratogenic effects, it can be used in the treatment of many infections of the genito-urinary tract.'[2]

Outlining the effect of antifungal therapy on BV, Menard remarks that self-treatment with antifungals is widely practiced and may be useful in women with Candida who are co-infected with BV as studies have shown that antifungal treatment cured the BV in 70% of women with simultaneous candida vaginitis. However he dismisses the widely held incorrect notion that opposing vaginal pH is required for the growth of C. albicans and BV, explaining that 'candida vulvo-vaginitis requires low acidity and BV requires high vaginal pH levels.' [2]

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EMERGING THERAPIES FOR BV USING METRONIDAZOLE

Menard and other authors confirm that the most common therapy in the treatment of BV is vaginal delivery of metronidazole or clindamycin. However, there are promising therapeutic developments aimed at improving existing formulations or creating new dosage forms. These include a group in Egypt focusing on pluronic polymers that has developed a hydrogel that swells in aqueous environments for use as a drug delivery system. Menard says 'this novel vaginal delivery system for metronidazole improved the therapeutic efficacy compared with that achieved with conventional vaginal gel.'

A new dosage form containing metronidazole is also being developed that includes bio adhesive polymers in vaginal muco-adhesive tablets. [2] 'The in vitro properties and antibacterial activity of these new formulations may offer an alternative to traditional dosage forms for vaginal topical administration.' [2]

Vulvovaginal Candidiasis (VVC)

Professor Paladine notes in her article that the treatment of candidal infection is aimed at reducing symptoms, highlighting the availability of 'several topical azole preparations and regimens as well as oral fluconazole (Diflucan) in a single 150-mg dose. She stresses that 'the choice of treatment should be made in conjunction with patient preference and previous experience with these agents' as there are also several considerations when choosing between topical and oral therapies. Short-course topical formulations (i.e., single dose and regimens of 1–3 days) effectively treat uncomplicated VVC.
The CDC's recommended regimes for vulvovaginal candidiasis are oral fluconazole and well as several topical treatments as first-line therapy.

RECOMMENDATIONS FOR DOCTORS [1] [6]

- Obtaining a medical history alone is insufficient to diagnose vaginitis accurately.
- Therefore, it is necessary to do a careful history, examination and laboratory testing to determine the aetiology of vaginal symptoms.
- Clinicians should elicit information on sexual behaviours and practices, gender of sex partners, menses, vaginal hygiene practices (e.g., douching) and self-treatment with medications.
- All women with BV should be tested for HIV and other STDs.

ADVICE TO GIVE PATIENTS

- Patients should abstain from using alcohol use for 24 hours after completion of treatment with oral metronidazole formulations to reduce the possibility of a disulfiram-like reaction
- Women should be advised to avoid sexual activity or use condoms consistently and correctly during the treatment regimen.
- Because persistent or recurrent BV is common, women should be advised to return for evaluation if symptoms recur.

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