2001 National guideline for the management of bacterial vaginosis

Clinical Effectiveness Group (Association for Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases)

Aetiology

Bacterial vaginosis (BV) is the commonest cause of abnormal discharge in women of childbearing age. The reported prevalence has varied from 5% in a group of asymptomatic college students to as high as 50% of women in Uganda. It was reported in 12% of pregnant women in the United Kingdom[1], and 30% of women undergoing termination of pregnancy[2]. It is characterised by an overgrowth of predominantly anaerobic organisms (*Gardnerella vaginalis, Prevotella species, Mycoplasma hominis, Mobiluncus species*) in the vagina, leading to replacement of lactobacilli and an increase in pH from less than 4.5 to as high as 7.0. It can arise and remit spontaneously in sexually active and non-sexually active women. It is more common in black women than white, those with an intrauterine contraceptive device, and those who smoke. It is not regarded as a sexually transmitted disease. The aetiology is not known.

Clinical features

Symptoms

Offensive fishy smelling vaginal discharge
Not associated with soreness, itching, or irritation
Many women (approximately 50%) are asymptomatic.

Signs

Thin, white, homogeneous discharge, coating the walls of the vagina and vestibule.

Complications

Although the incidence of BV is high in women with pelvic inflammatory disease (PID) there are no prospective studies investigating whether treating asymptomatic women for BV reduces their risk of developing PID subsequently. BV is common in some populations of women undergoing elective termination of pregnancy (TOP), and is associated with post-TOP endometritis and PID (level of evidence Ib)[3]. In pregnancy BV is associated with late miscarriage, preterm birth, preterm premature rupture of membranes, and postpartum endometritis (Ib)[4-6].

BV has been associated with an increased incidence of vaginal cuff cellulitis and abscess formation following transvaginal hysterectomy (III)[7], but it is unclear whether this is a problem in UK practice where many units administer perioperative antibiotics. There are no studies investigating the possible role of BV in the onset of PID following insertion of an intrauterine contraceptive device (IUCD). In one study BV was associated with NGU in male partners[8].

Diagnosis

In clinical practice BV is diagnosed using the Amsel criteria[9]. At least three of the four criteria are present for the diagnosis to be confirmed.

(1) Thin, white, homogeneous discharge

(2) Clue cells on microscopy

(3) pH of vaginal fluid >4.5

(4) Release of a fishy odour on adding alkali (10% KOH).

An alternative is to use a Gram stained vaginal smear, with the Hay/Ison criteria or the Nugent criteria. The Hay/Ison criteria are defined as follows:
grade 1 (Normal): Lactobacillus morphotypes predominate
grade 2 (Intermediate): Mixed flora with some Lactobacilli present, but Gardnerella or Mobiluncus morphotypes also present
grade 3 (BV): Predominantly Gardnerella and/or Mobiluncus morphotypes. Few or absent Lactobacilli[1].
The Nugent score is derived from estimating the relative proportions of bacterial morphotypes to give a score between 0 and 10. A score of <4 is normal, 4-6 is intermediate, and >6 is BV[10].

Isolation of Gardnerella vaginalis cannot be used to diagnose BV because it can be cultured from the vagina of more than 50% normal women (IIa). In research studies a high concentration of Gardnerella vaginalis is associated with the presence of BV (IIa)[11].

Management

General advice
Patients should be advised to avoid vaginal douching, use of shower gel, and use of antiseptic agents or shampoo in the bath (grade of recommendation C).

Treatment
Treatment is indicated for:
- Symptomatic women (A)
- Women undergoing some surgical procedures (A)
- Some pregnant women (A).

Women who do not volunteer symptoms may elect to take treatment if offered. They may report a beneficial change in their discharge following treatment.

Recommended regimens
Metronidazole 400-500 mg twice daily for 5-7 days (A)

or
Metronidazole 2 g immediately (A).

Alternative regimens
Intravaginal metronidazole gel (0.75%) once daily for 5 days (A)

or
Intravaginal clindamycin cream (2%) once daily for 7 days (A)

or
Clindamycin 300 mg twice daily for 7 days (A).

Rationale
All these treatments have been shown to achieve cure rates of 70-80% after 4 weeks in controlled trials using placebo or comparison with oral metronidazole[4;5;12-15]. Oral metronidazole treatment is established, usually well tolerated, and inexpensive (Ia). Dosage and duration used in trials have varied from 400 mg twice daily for 5 days to 500 mg twice daily for 7 days. The 2 g immediate dose may be slightly less effective at 4 week follow up (Ib).

Intravaginal metronidazole gel and clindamycin cream have similar efficacy (Ib), but the latter is more expensive. Theoretically, metronidazole has an advantage because it is less active against lactobacilli than clindamycin. Conversely, clindamycin is more active than metronidazole against most of the bacteria associated with BV.

Oral clindamycin has only been evaluated in one study with short term follow up, and in pregnant women (Ib, IIa). It is more expensive than metronidazole.

Caution
With metronidazole treatment alcohol should be avoided because of the possibility of a disulfiram-like action. There are no data on the risks from consuming alcohol with intravaginal metronidazole gel, but it is not recommended at present. Clindamycin cream can weaken condoms, which should not be used during such treatment. Pseudomembranous colitis has been reported with both oral clindamycin and clindamycin cream[16].

Allergy
Allergy to metronidazole is uncommon. Use 2% clindamycin cream for metronidazole allergic women.

Pregnancy and breast feeding
Meta-analyses have concluded that there is no evidence of teratogenicity from the use of metronidazole in women during the first trimester of pregnancy (Ia)[17-19].
The results of clinical trials investigating the value of screening for and treating BV in pregnancy have been conflicting. It is therefore difficult to make firm recommendations. In summary, three randomised controlled trials have shown a reduction in the incidence of preterm birth following screening for and treatment of BV in women with a history of prior idiopathic preterm birth or second trimester loss. However, this was based on a subgroup analysis in two studies[11;20], and all three studies used different treatments: metronidazole 500mg twice daily for 7 days[21]; metronidazole 400 mg twice daily for 2 days repeated after 4 weeks if indicated[11]; and a combination of metronidazole 250 mg and erythromycin 333 mg both three times daily for 7 days.[20].
The largest multi-centre RCT randomised 1953 asymptomatic women with BV to receive 2 Grams metronidazole or placebo, taken under supervision in the clinic, repeated at home 2 days later[22]. The course was repeated 4 weeks later. There was no difference in gestational age at delivery between the two groups, or in the sub-group of women with a prior preterm birth. Possible limitations of this study include the relatively late gestational age at which treatment was administered (mostly 20-24 weeks gestation), the short course of metronidazole administered, and the high number of women screened positive for BV who were nor randomised.

One further study has shown a benefit from treatment with oral clindamycin 300 mg bd for 7 days[23]. However, a cohort design was used rather than randomisation, which limits the value of the study for making treatment recomendations (IIa). The use of clindamycin cream to treat BV in the second trimester of pregnancy has not produced a reduction in preterm birth in two small studies (Ib)[6;24].

The results of further randomised controlled trials of screening and treating all pregnant women are awaited, but there are insufficient data to make such a recommendation at present. In conclusion, symptomatic pregnant women should be treated in the usual way (B). Asymptomatic pregnant women with a history of ‘idiopathic’ preterm birth or second trimester loss may be screened and treated with oral metronidazole 400 mg twice daily for 7 days, but current evidence does not support routine screening for BV.

Metronidazole enters breast milk and may affect its taste. The manufacturers recommend avoiding high doses if breast feeding. Small amounts of clindamycin enter breast milk. It is prudent therefore to use an intravaginal treatment for lactating women (C).

Termination of pregnancy (TOP)
One study has demonstrated a reduction in post-TOP infection by treating BV with oral metronidazole before termination (Ib)[3]]. Another has demonstrated a reduction in infective complications following the use of clindamycin cream[25] (Ib).There are no data on the effectiveness of treatment administered at the time of TOP. These two studies support screening for and treating BV with either metronidazole or clindamycin cream, to reduce the incidence of subsequent endometritis and PID (Ia).

Sexual partners
No reduction in relapse rate was reported from two studies in which male partners of women with BV were treated with metronidazole, one study of tinidazole, and one of clindamycin (Ib)[13;26]. Routine screening and treatment of male partners are therefore not indicated. One small study reported a high incidence of BV in female partners of lesbian women with BV (III)[27]. No study has investigated the value of treating partners of lesbian women simultaneously.

Follow up
A test of cure is not required if symptoms resolve. If treatment is prescribed in pregnancy to reduce the risk of preterm birth, a repeat test should be made after 1 month and further treatment offered if the BV has recurred.

Recurrent bacterial vaginosis
There are few published studies evaluating the optimal approach to women with frequent recurrences of BV. Small studies of live yoghurt or Lactobacillus acidophilus have not demonstrated benefit (IIa)[13].

Auditable outcome measures
Diagnosis of BV in clinical practice. Compare routine diagnosis with stored vaginal smears examined by Gram stain.
Screening and treatment of women undergoing termination of pregnancy. This should also include screening for *Chlamydia trachomatis* (see guideline for chlamydia).

Author and centre
Phillip Hay, St George's Hospital Medical School.

Membership of the CEG
Clinical Effectiveness Group: chairman, Keith Radcliffe (MSSVD); Imtyaz Ahmed-Jushuf (AGUM); Jan Welch (MSSVD); Mark FitzGerald (AGUM); Janet Wilson (Royal College of Physicians GU Medicine Committee).

Conflict of interest
Phillip Hay has worked as a consultant and investigator in trials for Upjohn and Pharmacia (2% clindamycin cream) and 3M Pharmaceuticals (0.75% metronidazole gel).

Evidence base
A Medline search was conducted using the terms "bacterial vaginosis" and "treatment" to identify treatment trials and reviews or meta-analyses. The 1994 and 1995-2000 databases were searched. Previous guidelines were sought, and the 1998 USA guidelines reviewed. The Cochrane database was searched using the term "bacterial vaginosis".

Reference List

1. Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. **Br Med J** 1994; **308**: 295-298.

2. Blackwell AL, Thomas PD, Wareham K, Emery SJ. Health gains from screening for infection of the lower genital tract in women attending for termination of pregnancy. **Lancet** 1993; **342**: 206-210.

3. Larsson PG, Platz-Christensen JJ, Thejls H, Forsum U, Pahlson C. Incidence of pelvic inflammatory disease after first-trimester legal abortion in women with bacterial vaginosis after treatment with metronidazole: a double-blind, randomized study. **Am J Obstet Gynecol** 1992; **166**: 100-103.

4. Hay PE. Therapy of bacterial vaginosis. **J Antimicrob Chemother** 1998; **41**: 6-9.

5. Centers for Disease Control and Prevention. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR 1998;47:1-118.

6. McGregor JA, French JI, Jones W, et al. Bacterial vaginosis is associated with prematurity and vaginal fluid mucinase and sialidase: results of a controlled trial of topical clindamycin cream. **Am J Obstet Gynecol** 1994; **170**: 1048-1059.

7. Soper DE. Bacterial vaginosis and postoperative infections. **Am J Obstet Gynecol** 1993; **169**: t-9

8. Keane FE, Thomas BJ, Whitaker L, Renton A, Taylor-Robinson D. An association between non-gonococcal urethritis and bacterial vaginosis and the implications for patients and their sexual partners. **Genitourin Med** 1997; **73**: 373-377.

9. Amsel R, Totten PA, Spiegel CA, Chen KC, Eschenbach D, Holmes KK. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. **Am J Med** 1983; **74**: 14-22.

10. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. **J Clin Microbiol** 1991; **29**: 297-301.

11. McDonald HM, O'Loughlin JA, Vigneswaran R, et al. Impact of metronidazole therapy on preterm birth in women with bacterial vaginosis flora (Gardnerella vaginalis): a randomised, placebo controlled trial [see comments]. **Br J Obstet Gynaecol** 1997; **104**: 1391-1397.

12. Anonymous. Management of bacterial vaginosis. **Drug & Therapeutics Bulletin** 1998; **36**: 33-35.

13. Larsson PG. Treatment of bacterial vaginosis. **Int J STD AIDS** 1992; **3**: 239-247.

14. Lugo-Miro VI, Green M, Mazur L. Comparison of different metronidazole therapeutic regimens for bacterial vaginosis. A meta-analysis. **JAMA** 1992; **268**: 92-95.

15. Hillier SL, Lipinski C, Briselden AM, Eschenbach DA. Efficacy of intravaginal 0.75% metronidazole gel for the treatment of bacterial vaginosis. **Obstet Gynecol** 1993; **81**: 963-967.

16. Trexler MF, Fraser TG, Jones MP. Fulminant pseudomembranous colitis caused by clindamycin phosphate vaginal cream. Am J Gastroenterol 1997;92:2112-3.

17. Burtin P, Taddio A, Ariburnu O, et al. Safety of metronidazole in pregnancy: a meta-analysis. Am J Obstet Gynecol 1995;172:525-9.

18. Caro-Paton T, Carvajal A, Martin de Diego I, et al. Is metronidazole teratogenic? A meta-analysis. Br J Clin Pharmacol 1997;44:179-82

19. Czeizel A, Rockenbauer M. A population based case-control teratologic study of oral metronidazole treatment during pregnancy. Br J Obstet Gynaecol 1998;105:322-7.

20. Hauth JC, Goldenberg RL, Andrews WW, DuBard MB, Copper RL. Reduced incidence of preterm delivery with metronidazole and erythromycin in women with bacterial vaginosis. **N Engl J Med** 1995; **333**: 1732-1736.

21. Morales WJ, Schorr S, Albritton J. Effect of metronidazole in patients with preterm birth in preceding pregnancy and bacterial vaginosis: a placebo-controlled, double-blind study. **Am J Obstet Gynecol** 1994; **171**: 345-347.

22. Carey JC, Klebanoff MA, Hauth JC, et al. Metronidazole to prevent preterm delivery in pregnant women with asymptomatic bacterial vaginosis. **N Engl J Med** 2000; **342**: 534-540.

23. McGregor JA, French JI, Parker R, et al. Prevention of premature birth by screening and treatment for common genital tract infections: results of a prospective controlled evaluation. **Am J Obstet Gynecol** 1995; **173**: 157-167.

24. Joesoef MR, Hillier SL, Wiknjosastro G, et al. Intravaginal clindamycin treatment for bacterial vaginosis: effects on preterm delivery and low birth weight. **Am J Obstet Gynecol** 1995; **173**: 1527-1531.

25. Larsson PG, Platz-Christensen JJ, Dalaker K, et al. Treatment with 2% clindamycin vaginal cream prior to first trimester surgical abortion to reduce signs of postoperative infection: a prospective, double-blinded, placebo-controlled, multicenter study. **Acta Obstet Gynecol Scand** 2000; **79**: 390-396.

26. Colli E, Landoni M, Parazzini F. Treatment of male partners and recurrence of bacterial vaginosis: a randomised trial. **Genitourin Med** 1997; **73**: 267-270.

27. Berger BJ, Kolton S, Zenilman JM, Cummings MC, Feldman J, McCormack WM. Bacterial vaginosis in lesbians: a sexually transmitted disease. **Clin Infect Dis** 1995; **21**: 1402-1405.