National Guideline For The Management Of Bacterial Vaginosis (2006)
Clinical Effectiveness Group
British Association for Sexual Health and HIV

Introduction and Methodology

Scope and Purpose

The main objective is to assist practitioners in managing women diagnosed with bacterial vaginosis.

This guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of bacterial vaginosis including the management of the initial presentation, as well as recurrence.

It is aimed primarily at people aged 16 years or older (see specific guidelines for those under 16) presenting to health care professionals, working in departments offering level 3 care in STI management (see national strategy[(2)]) within the United Kingdom. However, the principles of the recommendations should be adopted across all levels (levels 1 and 2 may need to develop, where appropriate, local care pathways).

Stakeholder Involvement

This guideline has been produced by medical specialists from relevant disciplines. Successive drafts have been reviewed by the clinical effectiveness group of BASHH.

Rigour of Development

An extensive literature reviewed was carried out using Medline for the years 1970 to 2005 using the keyword "bacterial vaginosis". The Cochrane library was searched using "bacterial vaginosis". Previous guidelines were sought, and the 1998 and 2002 USA guidelines reviewed.

Where available systematic reviews were used. Additionally,randomised clinical trials and review articles were referenced. Only English language papers were used. The previous 2001 guidelines were used as a basis. Where feedback from

clinicians indicated areas of controversy these were reviewed, and areas in which new RCTs had been published were reviewed. Expert opinion was sought for difficult areas such as the management of bacterial vaginosis in pregnancy.

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 rural Uganda. A prevalence of 12% was found in pregnant women attending an ante-natal clinic in the United Kingdom(1), and of 30% in women undergoing termination of pregnancy(2).

BV 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.

Spontaneous onset and remission of BV can occur. Whilst BV is not regarded as a sexually transmitted disease, the prevalence is generally higher amongst sexually active than non-sexually active women(3). It is more common in black women than white, those with an intrauterine contraceptive device, and those who smoke.

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

The prevalence of BV is high in women with pelvic inflammatory disease (PID), and in one prospective study BV was predictive of subsequent PID associated with gonorrhoea or chlamydia (4)(level of evidence 11a).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)(5). In pregnancy BV is

associated with late miscarriage, preterm birth, preterm premature rupture of membranes, and postpartum endometritis (Ib) (6-10).
BV has been associated with an increased incidence of vaginal cuff cellulitis and abscess formation following transvaginal hysterectomy (III)(11), 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(12).

Diagnosis

Two approaches are available

• Amsel criteria(13).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 of wet mount
(3) pH of vaginal fluid >4.5
(4) Release of a fishy odour on adding alkali (10% KOH).

• A Gram stained vaginal smear, evaluated with the Hay/Ison criteria(14) or the Nugent criteria(15).

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(15).

The Bacterial Special Interest group of BASHH recommend using the Hay/Ison criteria in Genitourinary medicine clinics. (grade of recommendation C).

• 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)(16).

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)

- 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 single dose (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).
Or
Tinidazole 2G single dose (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(6;7;17-20). 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. Tinidazole has similar activity to metronidazole but is also more expensive.

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(21).

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) (22-24).
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. A detailed discussion of trials in pregnancy is in the appendix. In conclusion:

- Symptomatic pregnant women should be treated in the usual way (B).

- There is insufficient evidence to recommend routine treatment of asymptomatic pregnant women who attend a G-U clinic and are found to have 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)

Three studies have investigated whether antibiotics can reduce the rate of infectious morbidity in women with BV, following termination of pregnancy. A Scandinavian study of 231 women demonstrated a reduction in post-TOP infection by treating BV with oral metronidazole before termination(5) (Ib). Another demonstrated a reduction in infective complications following the use of clindamycin cream(35) (Ib). A UK study of 273 women again found a reduction in post-operative upper genital tract infection from 16% to 8.5%, but did not quite reach statistical significance(36). There are no data on the effectiveness of treatment administered at the time of TOP.

- These 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(18;37) (Ib). Routine screening and treatment of male partners are therefore not indicated.

- Two studies reported a high incidence of BV in female partners of lesbian women with BV(38;39) (II). 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.

Recurrent bacterial vaginosis

There are few published studies evaluating the optimal approach to women with frequent recurrences of BV. Possible approaches are as follows:

- Suppressive therapy. Metronidazole gel 0.75%. twice weekly for 4 to 6 months to decrease symptoms, after an initial treatment daily for 10 days, is being evaluated.
- Metronidazole orally 400 mg bd for 3 days at the start and end of menstruation, combined with fluconazole 150 mg as a single dose if there is a history of candidiasis also (III).
- A recent observational study reported that acigel used at the time of menstruation and following unprotected sexual intercourse was associated with a reduction in relapse rate following a course of metronidazole(40)(III).
- Small studies of live yoghurt or Lactobacillus acidophilus have not demonstrated benefit (IIa)13.
- Other treatments being studied at present include the use of combinations of antibiotics with probiotic therapy and hydrogen peroxide.

Qualifying statement

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources.

All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

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).

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Editorial Independence

This guideline was commissioned and edited by the CEG of the BASHH, without external funding being sought or obtained. The author has declared potential conflicts of interest.

Appendix

Treatment of BV in pregnancy

In summary, three randomised controlled trials have shown a reduction in the incidence of preterm birth following screening for and treatment of BV with metronidazole 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(16;25), and all three studies used different treatments: metronidazole 500mg twice daily for 7 days(26); metronidazole 400 mg twice daily for 2 days repeated after 4 weeks if indicated(16); a combination of metronidazole 250 mg and erythromycin 333 mg both three times daily for 7 days(25).
The largest multi-centre RCT randomised 1953 asymptomatic unselected women with BV to receive two Grams metronidazole or placebo, taken under supervision in the clinic, repeated at home two days later(27). The course was repeated four 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 not randomised. A UK based study in which women with a high level of fetal fibronectin at 24 – 28 weeks gestation were treated with oral metronidazole 400 mg tds for 7 days, was terminated early with the conclusion that the treatment increased the rate of preterm delivery(28). Only 5 women in the placebo group and 8 in the treatment group had BV: BV only resolved in one subject after treatment was administered. There was a non-significant trend for metronidazole treatment to be associated with early preterm birth: 11/53 (21%) women who received metronidazole delivered before 30 weeks gestation of women receiving metronidazole compared to 5/46 (11%) of those receiving placebo (risk ratio 1.9, 95% CI 0.72–5.09, P = 0.18). There were significantly more preterm

deliveries (before 37 weeks) in women treated with metronidazole 33/53 (62%) than placebo 18/46 (39%) (risk ratio 1.6, 95% CI 1.05–2.4, p= 0.022). The authors have been quoted as stating that metronidazole should not be prescribed to pregnant women because it appeared to increase the risk of preterm birth in those with a history of prior preterm birth. Given that this was a selected group with positive fetal fibronectin, treated relatively late in pregnancy (> 24 weeks gestation), and that < 10% had BV this study does not provide sufficient data to say that metronidazole should not be used to treat BV in pregnancy. Moreover, the larger Carey study did not show an increase in preterm birth associated with metronidazole use at a similar gestational age(27).

One further study from the USA has shown a benefit from treatment with oral clindamycin 300 mg bd for 7 days(29). However, a cohort design was used rather than randomisation, which limits the value of the study for making treatment recommendations (IIa). More recently, a UK RCT found that treating asymptomatic women with BV or intermediate flora detected on Gram stain produced a five-fold reduction in late miscarriage and two and a half-fold reduction in spontaneous preterm birth(30). Treatment was clindamycin 300 mg twice daily at a median gestation of 15.8 weeks.
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)(8;31). Again a UK study reported a sixty percent reduction in spontaneous preterm birth using clindamycin cream 100 mg daily for three days, followed by a seven day course if BV persisted 4 weeks later{Lamont, Duncan, et al. 2003 1163 /id}. In a large Austrian RCT of antenatal screening for BV, candida and Trichomonas, Kiss and colleagues reported that screening and treatment for infections between 15 and 20 weeks gestation in 4429 women produced a preterm birth rate of 3% compared to 5.3% in the control group(32). Of the 177 women treated for BV with 2% clindamycin vaginal cream, 59 (29%) required retreatment with oral clindamycin for persistent BV after 28 weeks gestation. Numerically the majority of the benefit appeared to be in women treated for candidal infection. In the intervention group 6/175 women treated for BV had a spontaneous preterm birth compared to 10/176 in the control group (OR 0.59, 95% CI 0.17 – 1.54, p > 0.05).

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Declaration of Personal Interests

Name of guideline:

1. Do you, your partner (if applicable) or any member of your immediate family have any commercial interest such as personal shares etc. with any companies that are, or could be, involved in the above named guideline?

No

2. Do you, your partner (if applicable) or any member of your immediate family receive sponsorship or paid consultancy work within commercial organisations that are, or could be, involved in the above named guideline?

No

3. Does your department or unit receive financial support from commercial organisations that are, or could be, involved in the above named guideline?

No

4. Are you a consultant to or a member of any national body, charity or pressure group whose work is related to the above named guideline?

No

5. Do you receive significant editorial fees for commissioned articles for publication (in any format) or are you paid editorial work for any publication related to the above named guideline?

No

6. Do you or your department hold a patent (existing or pending) related to the above named guideline?

No

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Signature: date: 14 March 2006