

United Kingdom National Guideline on the Management of Vulvovaginal Candidiasis (2007)

Clinical Effectiveness Group British Association of Sexual Health and HIV

Introduction and Methodology

Scope and Purpose

The main objective is to assist practitioners in the management of uncomplicated and complicated Vulvovaginal Candidiasis.

This guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of Vulvovaginal Candidiasis.

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 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 physicians, including those with a specialist interest, with input from patients attending UK GUM clinics. The draft guideline was placed on the BASHH website for a three-month consultation period.

The process was overseen by the BASHH Clinical Effectiveness Group (CEG). This is the second revision of the guideline first published in 1999.

Rigour of Development

An extensive literature review was performed using Medline for the years 1966-2007. MEDLINE search-keywords: vulvovaginal candidiasis, vaginal candidosis, vaginal candida. The resulting articles were handsearched and sorted. Further references were obtained from these articles.

The Cochrane Library was searched; search-keywords were vulvovaginal candidiasis, vaginal candidosis, vaginal candida (2007).

Aetiology

Causative Agents

Candida albicans 80-92%^{1,2}

Non-albicans species e.g. *C. glabrata*, *C. tropicalis*, *C. krusei*, *C. parapsilosis*, and *Saccharomyces cerevisiae*

Clinical Features

Symptoms

Vulval itch

Vulval soreness

Vaginal discharge

Superficial dyspareunia

External dysuria

Signs

Erythema

Fissuring

Discharge, typically curdy but may be thin. Non-offensive

Oedema

Satellite lesions

Excoriation

None of these symptoms or signs are pathognomonic for vulvovaginal candidiasis; corroborative evidence of laboratory tests should be sought³ as many women (more than half of self-diagnosed women in one study⁴) may have other conditions e.g. dermatitis, allergic reactions, *lichen sclerosus*. In addition, symptoms/signs are no guide to species.^{3,5} 10-20% of women during reproductive years may be colonized with *Candida sp.*^{6,7} but have no clinical signs or symptoms. These women do not require treatment.

Vulvo-vaginal candidiasis is mostly uncomplicated unless the following are present, when it is regarded as complicated:

- Severe symptoms (a subjective assessment)
- Pregnancy
- Recurrent vulvovaginal candidiasis (more than 4 attacks per year)
- Non-albicans species
- Abnormal host (e.g. hyperoestrogenic state, diabetes mellitus, immunosuppression)

Diagnosis

In the context of comprehensive sexual health services, routine microscopy and culture is the standard of care for symptomatic women^{3;9-13} (Evidence level III, grade C)

A vaginal swab should be taken from the anterior fornix¹⁴ (Evidence level III, grade B) for the following:

- Gram or wet film examination^{3;9-13} (Evidence level III, grade B)
- Directly plated to solid fungal media. Speciation to albicans/non-albicans is strongly preferred if uncomplicated disease, and essential if complicated disease suspected/present¹⁵⁻¹⁸ (Evidence level III, grade B)

See British Association of Sexual Health and HIV Clinical Effectiveness Group guidelines 'Sexually Transmitted Infections: UK National Screening and Testing Guidelines', August 2006 for comprehensive guidance.

[www.bashh.org/guidelines/2006/sti_screening_guidelines_v14_0806.pdf]

Management

General Advice

Routine recommendation of use of vulval moisturisers as soap substitute and regular skin conditioner (permission may need to be given to the patient that this does not constitute “internal use”)

Avoid tight fitting synthetic clothing^{19;20}

Avoid local irritants e.g. perfumed products (Level of evidence: IV, grade C)

Treatment

Uncomplicated Vulvovaginal Candidiasis

Since all topical and oral azole therapies give a clinical and mycological cure rate of over 80% in uncomplicated acute vulvovaginal candidiasis, choice is a matter of personal preference, availability and affordability.^{21;22}

Nystatin preparations give a 70-90% cure rate in this situation.⁷ See later section if severe symptoms/signs. Topical azole therapies can cause vulvovaginal irritation and this should be considered if symptoms worsen or persist.

Topical Therapies

DRUG	FORMULATION	DOSAGE REGIMEN
Clotrimazole*	Pessary	500mg stat
Clotrimazole*	Pessary	200mg x 3 nights
Clotrimazole*	Pessary	100mg x 6 nights
Clotrimazole*	Vaginal cream (10%)	5g stat
Econazole**	Pessary (Ecostatin 1)	150mg stat
Econazole**	Pessary	150mg x 3 nights
Fenticonazole**	Pessary	600mg stat
Fenticonazole**	Pessary	200mg x 3 nights
Isoconazole*	Vaginal tablet	300mg x 2 stat
Miconazole**	Ovule	1.2g stat
Miconazole**	Pessary	100mg x 14 nights
Nystatin	Vaginal cream (100,000 units)	4g x 14 nights
Nystatin	Pessary (100,000 units)	1-2 x 14 nights

*Effect on latex condoms and diaphragms not known **Product damages latex condoms and diaphragms

Oral Therapies

*Avoid in pregnancy/risk of pregnancy and breastfeeding (Level of evidence: II, grade A^{7;21;22})

DRUG	FORMULATION	DOSAGE REGIMEN
Fluconazole*	Capsule	150mg stat
Itraconazole*	Capsule	200mg bd x 1 day

Sexual Partners

There is no evidence to support the treatment of asymptomatic male sexual partners in either episodic or recurrent vulvovaginal candidiasis.^{23;24}

(Level of evidence: I, grade A)

Follow-up

Unnecessary if symptoms resolve. Test of cure is unnecessary.

Complicated Vulvovaginal Candidiasis

Pregnancy

Asymptomatic colonization with *Candida* species is more common (30-40%)²⁵ and symptomatic candidosis is more prevalent throughout pregnancy. Colonisation with *Candida* species is not associated with low birth weight or premature delivery.²⁶

Treatment

Topical imidazoles should be used for symptomatic vulvovaginal candidiasis in pregnancy. There is no evidence to suggest asymptomatic women need to be treated.²⁷ There is no evidence that any one topical imidazole is more effective than another. Longer courses are recommended; a four-day course will cure just over 50% whereas a seven-day course cures over 90%.²⁷ Oral therapy is contraindicated. (Level of evidence: II, grade B²⁷)

Recurrent Vulvovaginal Candidiasis

Definition

- At least 4 documented episodes of symptomatic vulvovaginal candidiasis annually⁸, with at least partial resolution of symptoms between episodes
- Positive microscopy or a moderate/heavy growth of *C. albicans* should be documented on at least two occasions when symptomatic (Level of evidence: IV, grade C)

Prevalence

Approximately 5% of women of reproductive age with a primary episode of vulvovaginal candidiasis will develop recurrent disease.^{28;29}

Pathogenesis

Caused by host factors rather than a more virulent strain or reintroduction of the organism to the genital tract.³⁰ It is usually due to *C. albicans*. Host factors include persistence of Candida (as detected by PCR although culture-negative between attacks)³¹, uncontrolled diabetes mellitus, immunosuppression, hyperoestrogenaemia (including HRT and the combined oral contraceptive pill),^{19;25} disturbance of vaginal flora e.g. through use of broad-spectrum antibiotics,^{19;32} and a link to allergy (in particular allergic rhinitis)³³ and pro-inflammatory genetic markers.

There is no evidence that iron deficiency is implicated.³⁴ One study³⁴ reported a statistically significantly lower serum level of zinc, magnesium and calcium in patients with recurrent vulvovaginal candidiasis, although all levels were within the normal range; other studies have refuted the link with serum zinc levels.³⁵

Further Investigation

Speciated fungal culture

FBC, random blood glucose only if other indicators (Level of evidence: IV, grade C)

General Advice

- As per uncomplicated disease.
- Vulval emollients may give symptomatic relief as vulval dermatitis both secondary and primary is commonly present.
- Review contraception. Avoid high-oestrogen contraceptives. Low oestrogen pills do not highly predispose to vulvovaginal candidiasis but may possibly have a negative influence on relapsing episodes³⁶.
- Consider use of Depo-Provera³⁷. (Grade of evidence: III, grade B)
- Lack of evidence for desogestrel-only pill (Cerazette) but would be logical alternative. (Grade of evidence: IV, grade C)

Treatment

The principle of therapy involves an induction regimen to ensure clinical remission, followed immediately by a maintenance regimen.

Recommended Regimen

TREATMENT STAGE	DRUG	FORMULATION	DOSAGE REGIMEN
Induction	Fluconazole*	Capsule	150mg every 72 hours x 3 doses
Maintenance	Fluconazole*	Capsule	150mg once a week for 6 months

*Avoid in pregnancy/ risk of pregnancy and breastfeeding

Approximately 90% of women will remain disease-free at 6 months and 40% at 1 year.
(Level of evidence: Ib, grade A³⁸)

Alternative Regimens

Induction

Topical imidazole therapy can be increased to 10-14 days according to symptomatic response.

(Level of evidence: IV, grade C)

Maintenance

DRUG	FORMULATION	DOSAGE REGIMEN
Clotrimazole	Pessary	500mg once a week
Fluconazole*	Capsule	50mg daily
Itraconazole*	Capsule	50-100mg daily
Ketoconazole*	Capsule	100mg daily

*Avoid in pregnancy/risk of pregnancy and breastfeeding

Cautions:

- Risk (low) of idiosyncratic drug-induced hepatitis, particularly with itraconazole and ketoconazole.
- These regimens are unlicensed for the indication.
- Anecdotal reports of oral contraceptive failure with prolonged oral azole therapy.

Maintenance therapy should last six months; 90% of women should remain disease-free during treatment.

(Level of evidence: IIa, grade B³⁹⁻⁴¹)

If relapse between doses consider twice-weekly 150mg fluconazole or 50mg fluconazole daily.

(Level of evidence: IV, grade C)

Alternatively consider the addition of cetirizine 10mg od.⁴²

There are no trials addressing the optimal duration of suppressive therapy. If recurrences after maintenance regimen are infrequent, each episode should be treated independently.

If recurrent disease is re-established the induction and maintenance regimens should be repeated.

(Level of evidence: IV, grade C)

Alternative Treatments

Probiotics/Lactobacillus

Evidence does not support use of oral or vaginal lactobacillus for the prevention of vulvovaginal candidiasis.^{43;44} Adverse effects from their use are extremely infrequent however and there are anecdotal reports of benefit. The mode of action might be via modulation of inflammatory processes⁴⁵ rather than due to a competitive effect with candida.

Diet

There is insufficient evidence to make any dietary recommendations, including on carbohydrate or yeast intake.^{8;46}

Role of Allergy

Zafirlukast 20mg bd for 6 months⁴⁷ may induce remission. Zafirlukast may be considered as maintenance prophylaxis for recurrent vulvovaginal candidiasis, particularly in women with a history of atopy.⁴² Cetirizine 10mg daily for 6 months⁴² may cause remission in women who fail to get complete resolution of symptoms with suppressive fluconazole.

(Level of evidence: IIb, grade B)

Tea tree oil (and other essential oils)

Are antifungal in vitro⁴⁸⁻⁵⁰ but may cause hypersensitivity reactions.⁵¹ Insufficient evidence to recommend use in recurrent vulvovaginal candidiasis.

Severe Vulvovaginal Candidiasis

Regardless of a history of recurrence, fluconazole 150mg should be repeated after three days as this improves symptomatic response but not recurrence.⁵²

(Level of evidence: Ib, grade A).

There is no benefit of 7-day local treatment over a single oral dose of fluconazole.⁵³ so if oral treatment is contra-indicated it is more logical to repeat a single dose pessary after three days. (Level of evidence: IV, grade C)

Low-potency corticosteroids are also thought by some experts to improve symptomatic relief in conjunction with adequate antifungal therapy

(Level of evidence: IV, grade C)⁸

Diabetes Mellitus

Symptomatic vulvovaginal candidiasis is more prevalent in diabetics and most problematic in those with poor control. Increased prevalence of species other than *C albicans*, in particular *C glabrata*.^{54;55} Glycaemic control should be optimized. When *C albicans* is isolated, single-dose fluconazole (150mg) gives a similar response to non-diabetics.⁵⁵

(Level of evidence: IIb, grade B)

Symptomatic women with *C glabrata* isolated: boric acid 600mg intravaginal suppository once a day for 14 days is as effective as fluconazole 150mgs stat⁵⁶
(Level of evidence: Ib, grade A)

HIV Infection

Vulvovaginal candidiasis occurs more frequently and with greater persistence in HIV-infected women.⁵⁷ Treat by conventional methods including use of suppressive antifungal regimens if necessary.⁵⁸
(Level of evidence: III, grade B)

Non-Albicans Species

Majority are *Candida glabrata* and are still susceptible to available azoles⁵⁹ although most non-albicans species have higher MICs. *Candida krusei* is intrinsically resistant to fluconazole.⁶⁰

In general for non-albicans infection longer courses may be needed although there is no data on optimum duration; two weeks is suggested. There no comparative evidence for different treatments.

Suggested alternatives include:

Nystatin pessaries are the only licensed alternative to azole therapy and are therefore the usual first line treatment for non- albicans infection. Unfortunately there are ongoing problems with supply (June 2008) and in this case consider local pharmacy production of Amphotericin B vaginal suppositories 50mg once a day for 14 days which is has a 70% success rate⁶¹
(Level of evidence: III, grade B)

Boric acid vaginal suppositories 600mg daily for 2-3 weeks.^{59;62} If mucosal irritation occurs the dose can be reduced to 300mg daily.⁶³ There is still limited evidence for this drug. There may be a teratogenic risk.⁶⁴
(Level of evidence: III, grade B)

Intravaginal flucytosine (5g cream or 1g pessary) either separately^{59;65} or with amphotericin⁶⁵ to reduce the chances of resistance (for which there is a low genetic barrier) can be used for two weeks.
(Level of evidence: III, grade B)

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 judgment of the clinician and consideration of individual patient circumstances and available resources.

All possible care has been taken 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.

Applicability

The diagnosis of VVC is syndromic. Diagnostic criteria may therefore vary with the clinical setting. It is acknowledged that some tests, e.g. for precise speciation of *Candida*, may not be available in all settings.

Some preparations e.g. flucytosine cream may not be available on local formularies. It is advised that such preparations are discussed with the unit pharmacist prior to prescribing.

Auditable Outcome Measures

- Cheapest acceptable topical/oral treatment option to be used in non-pregnant women. Target: 80%.
- All women with severe symptoms should receive fluconazole 150mg repeated after 3 days (unless contraindicated). Target: 100%
- All women with proven recurrent vulvovaginal candidiasis should be offered suppressive or alternative long term therapy. Target: 100%
- Asymptomatic male partners should not be treated. Target: 100%.

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Conflict of Interest

David White: None

Claire Robertson: None

Evidence Base

MEDLINE search-keywords: vulvovaginal candidiasis, vaginal candidosis, vaginal candida (1966 – 2007)

COCHRANE LIBRARY search-keywords: vulvovaginal candidiasis, vaginal candidosis, vaginal candida (2007)

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