MANAGEMENT OF RECURRENT VULVOVAGINAL CANDIDIASIS

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ABSTRACT

Backgound:
Recurrent vulvovaginal candidiasis (VVC) is a common problem amongst women, frequently encountered in primary care. However, there is paucity of clinical guidelines on its management.

Objective:
This article serves to look at the studies which have been done in the management of recurrent vulvovaginal candidiasis. The diagnosis, etiology, and treatment options will be discussed.

Methods:
A Pubmed search was conducted in August 2007. In addition, relevant articles were also searched via OVID, key journals, and hand search of referenced articles quoted in the papers.

Results:
In patients with recurrent VVC, mycological diagnosis is needed for confirmation of diagnosis and to exclude resistant species. Identifiable reversible risk factors should be corrected. The initial treatment usually involves a prolonged course of either oral or intravaginal antifungal agents. This is followed by a six-month maintenance regimen, with intravaginal or oral antifungal agents. It is effective in reducing the number of episodes of vulvovaginal candidiasis during the six months treatment period. However, recurrence is common with cessation of therapy.

Conclusion:
There is currently no effective treatment for long term cure of recurrent vulvovaginal candidiasis. Maintenance prophylactic antifungal regimens, however, can be employed to reduce the episodes or recurrences. Considering the side effect profile and cost effectiveness of the various maintenance antifungal regimens, intravaginal antifungal agent seems to be a reasonable therapeutic option. Behavioural risk factors modification, though of doubtful benefits, can be advised. Although there is limited evidence for the use of probiotics, its use can be advocated since the adverse effects are rare.

Keywords: **recurrent vulvovaginal candidiasis, topical antifungal agents, oral antifungal drugs.**

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INTRODUCTION

Recurrent vulvovaginal candidiasis (VVC) is defined as four or more proven episodes of vulvovaginal candidiasis in the past one year[1,2]. 75% of the female population will have at least one episode of candida vulvovaginitis during their lifetime. 40-50% will have recurrent episodes. Recurrent VVC occurs in 5% of healthy woman[3,4].

Recurrent VVC frustrates both the patient and the doctor. It causes much physical discomfort to the patient and poses a therapeutic challenge to the physician. However, to date, there is no consensus on its management.

This article serves to help the family physician deal with this common condition encountered in primary care. Confirmation of diagnosis is essential. Various predisposing factors have been suggested and will be discussed. In the treatment of recurrent VVC, the initial episode needs to be treated adequately, followed by a maintenance antifungal regimen. There are various antifungal regimens which will be discussed. Complementary therapy, though of unproven benefits, will be reviewed.

METHODOLOGY

Several search strategies were employed to achieve a comprehensive set of useful articles. The search was conducted 22 – 26 August 2007. A Pubmed search was done for review, meta-analysis, practice guideline, and randomised controlled trials from articles published in the last 10 years using the search keywords "Recurrent vaginal candidiasis" OR "Recurrent vulvovaginal candidiasis" OR "Chronic vaginal candidiasis" OR "Chronic vulvovaginal candidiasis". This yielded 19 articles. Ten articles (seven full text and three abstracts) were selected based on the relevance of topic and content. Using OVID, EBM reviews (including Cochrane Database of Systemic Reviews, ACP Journal Club, Database of Abstracts of Reviews of Effects, and Cochrane Central Register of Controlled Trials) on recurrent vulvovaginal candidiasis were screened and six articles were chosen. An additional three relevant journal articles were also obtained from journals from OVID. Search of key journals, e.g. American Journal of Obstetrics and Gynaecology, Genitourinary Medicine, yielded another nine articles. Finally, hand searching of relevant referenced articles quoted in the review articles yielded another six articles. A total of 34 articles were reviewed. The information collected were collated and organised.

DIAGNOSIS

Predominant symptoms of vulvovaginal candidiasis include intense vulva pruritus, and abnormal vaginal discharge (which

may be minimal, a thick "curd-like" material, or a watery secretion). The vulva may be erythematous, edematous, and contain satellite lesions. There may be burning sensation with urination. Rarely is vulva candidiasis seen without concomitant vaginal candidiasis[3].

Very often, vulvovaginal candidiasis is diagnosed without physical examination and without lab confirmation. However, the symptoms and signs may sometimes be non specific and studies have shown that the reliability of self-diagnosis is poor.[2]

Diagnosis of vulvovaginal candidiasis can be made with patient's history, clinical examination, supported by laboratory test of normal vaginal pH and yeast identified microscopically. In a patient with compatible clinical syndrome, who has yeast identified microscopically, a culture is usually not required. However, in patients with recurrent vulvovaginal candidiasis, culture should be obtained to exclude resistant organism[2]. Not infrequently, mixed infections can also occur, e.g. bacterial and concomitant candida infection[2].

ETIOLOGY

Causative organisms

Candida albicans is responsible for majority of symptomatic episodes. Nonalbicans species, e.g. Candida glabrata, accounts for 10-20% of the cases. However, the cases of nonalbicans infection have noted to be increasing. One of the possible reasons could be due to increased use of over the counter antimycotics. They may be used inappropriately, with short incomplete course, thus eliminating the more sensitive Candida albicans and selecting the more azole-resistant non albicans candida species[2].

Pathophysiology

There has been a paradigm change in the belief of the pathogenesis of VVC. Instead of VVC being caused by a defective immune system, there is data to suggest that symptomatic VVC is associated with an aggressive response by polymorphonuclear cells[5].

Interestingly, recurrent vulvovaginal candidiasis has also been found to be associated with perennial allergic rhinitis, suggesting a possible allergic link to its pathogenesis[6]. It has been proposed that recurrent VVC could be a hypersensitivity response to Candida[7].

Predisposing factors to recurrent Vulvovaginal Candidiasis (Table 1)

Traditionally, uncontrolled diabetes, steroid use, antibiotic use, immunosuppression have been known to be predisposing factors for recurrent VVC. However, very often, patients with recurrent VVC do not have these recognisable factors. Other proposed predisposing factors include sexual practices (e.g. oral-genital contact), excessive douching, extended use of panty liners, dietary factors. However, studies to date have yielded contradictory results.

Table 1. Predisposing factors to recurrent vulvovaginal candidiasis[2,3,10]

1. Uncontrolled diabetes
2. Steroid use
3. Antibiotic use- exact mechanism unknown
4. Immunosuppression
5. Behavioural factors
   – sexual practices
   – contraception (IUCD use)
   – douching and feminine products
6. Anecdotal, unproved factors
   – extended panty liner use
   – tight fitting clothing, synthetic underwear
   – dietary factors

Behavioural factors

Sexual factors

The relation of recurrent VVC to the frequency of coitus remains controversial. However, frequent oral-genital contact appears to increase its risk[8,9].

The possible reason could be due to contact transmission. One third of adult population is said to harbor oral candida albicans, and direct contact transmission is possible. Another proposed pathophysiology is that saliva may promote growth of candida through moistening and irritation of the vulva mucosa. It could also change the local immunological state resulting in susceptibility to candida infection[8].

However, in another study, sexual practices showed no association[10].

Contraception

– IUCD

Intrauterine contraceptive device (IUCD) usage has been associated with a higher risk of recurrent VVC[3]. The IUCD threads can act as pathogen reservoir, making eradication difficult[4].

– Oral contraceptives

The risk of infection is greater with use of high estrogen containing first generation oral contraceptives (75-150mcg estrogen). New low dose oral contraceptives are unlikely to contribute to candida infection. Hence, discontinuing their use is generally not necessary[3]. Some anecdotal reports have indicated, however, that cessation of oral contraceptive use occasionally resolves the infection in frustrating cases[3].

Douching and feminine products

The normal vaginal pH is 3.8-4.4. The production of lactic acid by Lactobacilli is involved with maintaining a normal pH, protecting against vaginal pathogens. Douching and menstruation alter the vaginal pH[3]. However, studies have failed to establish an association between douching and vaginal candidiasis[2].

Anecdotal, unproved factors

Extended panty liner use

In a prospective study of 65 women more than 18 years of age with recurrent VVC, results showed positive association between vulvovaginal candidiasis and panty liner use. In the week of a VVC episode, the relative risk of panty liner usage vs. non usage was 3.3 (95% CI 1.7-6.2). And in the week before a symptomatic episode, the relative risk for panty liner use was 2.3 (95% CI 1.2-4.3)[10]. However, in another study, a six-month prospective trial in 204 women that compared daily panty liner use to no use found no increase in the prevalence of cell densities of candida and no evidence for symptomatic infection[11].

The use of sanitary napkins, tampons, tight-fitting clothing, and synthetic underwear have also been proposed to be predisposing factors for recurrent VVC[3,4].

Dietary factors

Most studies to date have failed to show that dietary excesses or deficiencies play a major role. The role of consumption of excess unrefined sugars to the risks of recurrent VVC remained controversial. Maintaining a yeast free diet to decrease the risk of recurrent VVC, has had no supportive data of proven benefit[2].

TREATMENT OF RECURRENT VULVOVAGINAL CANDIDIASIS

Before making the diagnosis of recurrent vulvovaginal candidiasis, physicians must be aware that misdiagnosis is rather common. Hypersensitivity reactions and chemical or allergic reactions to topical antimycotic therapy can result in perpetuation of symptoms incorrectly thought to be caused by fungi. Fungal culture should be done for microbial confirmation and species identification[2,12-14].

Exogenous factors should be corrected. Diabetic control need to be optimised. Systemic corticosteroids should be avoided.

After mycological confirmation of diagnosis, the acute episode of vulvovaginal candidiasis has to be adequately treated.

Antifungal Agents for treatment of uncomplicated vulvovaginal candidiasis (Table 2)

For acute episodes of VVC in non-pregnant women, oral and intravaginal antifungal agents were equally effective[15,16]. Intravaginal antifungal agents are the first-line of therapy, but oral agents are sometimes associated with better compliance and they were found to be the preferred route of treatment by patients[16].

Intravaginal Antifungal Agents

Intravaginal antifungal agents are the most commonly used for initial treatment of uncomplicated vulvovaginal candidiasis. They have few adverse effects. Occasionally, local effects such as vaginal burning, stinging or irritation may occur[3].

Intravaginal antifungal agent is the therapeutic agent of choice in pregnancy. Both intravaginal azoles and intravaginal nystatin can be used in the first trimester of pregnancy[2,17].

Oral Antifungal Drugs

In a study comparing single oral dose of fluconazole vs. conventional intravaginal clotrimazole therapy of candida vaginitis, responses were similar in both groups and side effects were mild in both groups[18]. Hence, single dose of 150mg fluconazole was concluded to be as safe and as effective as conventional 7 days of intravaginal clotrimazole therapy.

A recent randomised controlled trial also found no statistically significant differences in the clinical and mycological efficacy between intravaginal clotrimazole (200mg for 3 days) and fluconazole (150mg single dose) in the treatment of both uncomplicated and recurrent vulvovaginal candidiasis[19]. However, the onset of symptomatic relief in the first 24 hours of treatment was significantly higher in the fluconazole than in the clotrimazole group.

However, whilst using oral antifungal agents for treatment of VVC, the risks of side effects and drug interactions have to be borne in mind[15]. Oral antifungal agents should generally be reserved for patients who are intolerable to intravaginal antifungal agents.

Maintenance Antifungal Treatment for Recurrent Vulvovaginal Candidiasis

In recurrent VVC, it is important that the current infection is treated effectively[1]. It is recommended that women with recurrent VVC prescribed a longer course of antifungal therapy to ensure clinical remission,[1,2] e.g. 3 doses of oral fluconazole 150mg every 72 hrs[20], or oral ketoconazole 400mg per day for 14 days[21]. This is followed by a maintenance regimen[2,14]. (Table 3)

Maintenance regimens should last at least six months. It is effective in preventing symptomatic recurrences, however recurrences is common immediately after cessation of the six-month regimen[2].

Oral antifungal maintenance therapy (Table 4)

Fluconazole

Fluconazole is effective for candida albicans and some non albicans, but is only 50% effective for candida glabrata[3]. Side effects include nausea, vomiting (3-4%), hepatotoxicity (hence liver function test should be checked after six months) and alopecia[3].

In a randomised double blind placebo controlled study by Sobel et al[20], (Table 4) it found that long term weekly fluconazole suppresses but does not cure recurrent vulvovaginal candidiasis. The study included women with active acute vulvovaginal candidiasis with a minimum of four documented episodes in

Table 2. Antifungal Agents for treatment of vulvovaginal candidiasis[3]

Intravaginal Antifungal Agents for treatment of vulvovaginal candidiasis		
Drug	**Formulation**	**Dosage Regimen**
Clotrimazole (Canestan, Cristan, Cotren)	100mg vaginal tablets	1 tablet x 6 days or 2 tablets x 3 days
	500mg vaginal tablets	Single dose
Isoconazole nitrate (gynotravagem)	600mg vaginal tablet	Single dose
Nystatin Pessary	100,000iu pessary	1 pessary x 14 days
Metronidazole 500mg and Nystatin 100,000iu (Flagystatin)		1 ovule nightly x 10 nights
Oral Antifungal drugs for treatment of vulvovaginal candidiasis		
Fluconazole (Difflucan)	150mg	Single dose
Itraconazole (Sporanox)	100mg	100mg om x 3 days
Ketoconazole (Nizoral)	200mg	200mg-400mg om x 5 days

Table 3. Antifungal maintenance regimens for recurrent vulvovaginal candidiasis[2,3,13,18,20-25]

Oral antifungal maintenance regimens for recurrent vulvovaginal candidiasis

- Fluconazole - 150mg once weekly for 6 months[3,20]
- Ketoconazole - 100mg daily for 6 months[13,21] or
  400mg x 5 days with onset of menses for 6 months[13,21]
- Itraconazole - 200mg once a month for 6 months[13,22] or
  200mg bd x 1 day on day 5 of menses for 6 months[23]

Intravaginal antifungal maintenance regimes for recurrent vulvovaginal candidiasis

- Clotimazole - 500mg pessary once a week for 6 months[2,3,18] or
  500mg pessary once a month on day 5 of menses[3,24] for 6 months or
  500mg pessary at onset of symptoms for 6 months[24] or
  2 x 100mg pessary twice a week for 6 months[13,25]

the previous 12 months. After treatment for acute symptoms with three doses of oral fluconazole 150mg every 72 hrs, 387 women were randomly assigned to receive oral fluconazole, 150mg weekly, or placebo for six months.

The result of vaginal cultures revealed no cases of fluconazole-resistant Candida albicans infection, and no evidence of superinfection with candida glabrata. Fluconazole was well tolerated. Therapy was discontinued only for one patient because of headache. Liver function test was monitored, only one participant had mildly elevated serum aminotransferase level.

The study concluded that recurrent VVC can be successfully and safely controlled by weekly suppressive therapy with fluconazole. However, long term cure is difficult to achieve as most patients (57.1%) had recurrent symptoms within six months of discontinuing therapy.

Ketoconazole

The side effects include hepatotoxicity, which is estimated to be 1/10,000 patients[3]. Hence, liver function test should be performed monthly[3]. Sobel et al[13,21] studied the efficacy of maintenance ketoconazole therapy in recurrent vulvovaginal candidiasis (Table 4). 74 women with recurrent VVC were treated for an acute episode with 400mg ketoconazole per day for 14 days. They were then randomised to receive one of the three treatment regimens: placebo or oral ketoconazole 400mg for five days with onset of menses for six months or oral ketoconazole 100mg daily for six months. The study concluded that maintenance prophylactic therapy with oral ketoconazole is effective in preventing recurrent episodes of vulvovaginal candidiasis, but relapse is common after withdrawal of the drug. Because of the risk of hepatotoxicity, caution is essential in selecting patients for long term ketoconazole therapy and in following patients undergoing such treatment[21].

Itraconazole

Liver function test monitoring is needed too[3]. A study reviewed the effectiveness of one day intermittent monthly prophylaxis with 400mg itraconaozle[23] (Table 4). It was a randomised study involving 57 patient and 57 controls. Results showed monthly itraconazole prophylaxis reduced the rate of recurrence, 36.4% (treatment group) vs. 64.5% (placebo group). However, its beneficial effects are lost within few months of cessation of therapy. After one year, only 38.9% of patients in the treatment group and 28.8% in the placebo group had no recurrence of symptoms.

In summary, the various oral antifungal maintenance regimen yielded the same findings, that it is effective in reducing the number of episodes during the six months treatment period. However, recurrences is almost 50% after cessation of therapy.

For patients with recurrence of symptoms with cessation of maintenance therapy, this can be treated initially as for uncomplicated acute vulvovaginal candidiasis[1]. However, if infection is recurrent, the treatment process should be repeated[1,2]. In such instances, Sobel[1,12] recommends keeping the maintenance regimen for 12 months.

Intravaginal Antifungal maintenance therapy (Table 4)

Intravaginal Clotrimazole pessary

In a prospective randomised open cross over study, looking at the value of prophylactic (monthly, perimenstrual) clotrimazole vs. empiric self treatment in recurrent vaginal candidiasis, empiric self treatment was found to be more cost effective than cyclical monthly use of pessary[24] (Table 4).

In this study, patients were randomised to receive one 500mg dose of clotrimazole pessary intravaginally each month just before or on the last day of menses for six months or one 500mg dose of clotrimazole intravaginally at the onset of symptoms for six months. After six months, patients were crossed over to the other regimen.

Table 4. Studies on Antifungal Maintenance Therapy for Recurrent Vulvovaginal Candidiasis[20,21,23-26]

Oral antifungal maintenance therapy				
		% with no recurrence 6 months post therapy	**% with no recurrence 12 months post therapy**	**Conclusion & Remarks**
Sobel et al. Maintenance fluconazole therapy for recurrent vulvovaginal candidiasis[20].	Fluconazole (150mg weekly for 6 months)	90.8%	42.9%	Long term weekly fluconazole reduced the rate of recurrent VVC, and is an option for suppressive therapy. However, most patients (57.1%) had recurrent symptoms within 6 months of discontinuing therapy.
(-387 patients)	placebo	35.9% (p<0.001)	21.9% (p<0.001)	
Sobel et al. Recurrent vulvovaginal candidiasis. A prospective study of the efficacy of maintenance ketoconazole therapy[21].	Ketoconazole (-400mg daily for 5 days with onset of menses for 6 menstrual cycle)	71.4% (p<0.01)	42.9% (-p>0.05)	It appears that maintenance prophylactic therapy with oral ketoconazole is effective in preventing recurrent episodes of vulvovaginal candidiasis, but that relapse is common after withdrawal of the drug
(-74 patients)	Ketoconazole (100mg daily for 6 months)	95.3% (-p<0.001)	52.4% (p<0.05)	
	placebo	28.6%	23.8%	
Spinillo et al. Managing recurrent vulvovaginal candidiasis. Intermittent prevention with itraconazole[23].	Itraconazole (400mg monthly for 6 months)	63.6%	38.9%	Monthly itraconazole prophylaxis reduced the rate of recurrence, however its beneficial effect is lost within months of cessation of therapy
(-114 patients)	placebo	35.5%	28.8% (p=0.83)	
Intravaginal antifungal maintenance therapy				
		Number of episodes end of 6 months		
Fong IW. The value of prophylactic (monthly) clotrimazole versus empiric self treatment in recurrent vaginal candidiasis[24].	Clotrimazole pessary 500mg (single dose) Just before or during the last day of menses	50 episodes (-mean of 2.2 episodes per patient) 188 pessaries used		Empiric self treatment with clotrimazole pessary is more cost effective than cyclical monthly use of pessary.
(23 patients)	At onset of symptoms	86 episodes (mean of 3.7 episodes per patient) 84 pessaries used		
Oral vs. Intravaginal Antifungal maintenance therapy				
		% with no recurrence 6 months post therapy	% with no recurrence 12 months post therapy	
Lopez et al. Treatment of recurring vulvovaginal candidiasis: A comparative prospective study during 6 months of 3 antimycotic preparations of single dose[25].	Fluconazole 150mg (19 patients)	52.63%	42.11%	Recurrent VVC needs early prophylaxis with one of this regimens and to maintain support at least one year for the benefit of the patient.
	Itraconazole 200mg (14 patients)	85.71%	64.28%	
(45 patients)	Clotrimazole pessary 500mg (11 patients) Day 6 menstrual cycle	91.66% (-p <0.05)	58.33% (No significant differences)	
Fong IW. The value of chronic suppressive therapy with itraconazole versus clotrimazole in women with recurrent vaginal candidiasis[26]	Itraconazole 200mg twice weekly for 6 months (1 patient did not complete study)	66.7% (-14/21)	52.4%	Intermittent suppressive therapy with clotrimazole pessary was more effective than itraconazole in preventing recurrent candida vaginitis, provided patients adhered to the regimen. Recurrence of vaginitis was common with both regimens after stopping suppressive therapy.
(44 patients)	Clotrimazole pessary 200mg twice weekly for 6 months (5 patients did not complete study)	100% (17/17) (p=0.02)	36% (p=0.15)	

There were more episodes of symptomatic vaginitis in the empiric treatment group. (3.7 episodes per patient in the empirical group vs. 2.2 episodes per patient in the monthly prophylactic group). However, during the prophylactic period, the empirical treatment group uses much lesser doses of clotrimazole (3.6 doses of clotrimazole in the empirical group vs. 7.3 doses in the prophylactic group). 74% of the patients preferred the empiric regime.

The authors of the study concluded that although prophylactic perimenstrual clotrimazole therapy may reduce the number of symptomatic episodes, empiric self-treatment is more cost effective and acceptable to patients.

Choice of anti-fungal preparation for treatment of recurrent vulvovaginal candidiasis; oral vs. intravaginal route

In a study by Lopez et al, three antimycotic preparations were compared in the treatment of recurrent vulvovaginal candidiasis[25] (Table 4). A total of 45 women with recurrent VVC were treated at random with a single dose of oral fluconazole 150mg (19 cases) or itraconazole 200mg (14 cases) or clotrimazole 500mg intravaginal pessary (11 cases), the sixth day of the menstrual cycle. Vaginal cultures were performed for identification of candida species, before and at six months of the treatment.

Vaginal pessary yielded the highest response rate of 91.66%. However, one year after the start of treatment, there was no significant difference in the response rates amongst the three treatment groups. Half the patients have recurrence of the symptoms.

In another study looking at oral itraconazole vs. intravaginal clotrimazole pessary in 44 women with recurrent vaginal candidiasis[26] yielded the following conclusion. Intermittent suppressive therapy with intravaginal clotrimazole (200mg daily for five days, then twice weekly for six months) was more effective than itraconazole (200mg daily for five days, then twice weekly for six months) in preventing recurrent candida vaginitis. Recurrence of vaginitis was common with both regimens after stopping suppressive therapy[26] (Table 4).

Currently, there is lack of large scale randomised controlled trials comparing the effectiveness and safety of each of the antifungal maintenance regimen. However, from the above studies, it seemed to show that a maintenance regimen with intravaginal antifungal agents is comparative to that of oral antifungal agents. However, recurrence rate is similar for both oral and intravaginal antifungal maintenance regimen after the six months treatment period.

Possible Future Pharmacotherapeutic Agents

The current therapeutic regimens do not seem to "cure" the patient of the disease. Recurrence is common with cessation of treatment. New immunotherapeutic strategies to control vaginal candidiasis is currently being studied[27] .

As mentioned earlier, recurrent VVC has been linked to allergic disease, particularly allergic rhinitis. In a small pilot open label study on the effect of Zafirlukast for severe recurrent vulvovaginal candidiasis, out of 20 women, 14 patients (70%) showed subjective response, six (30%) showed complete response. Seven (37%) remained symptom free 12 months after stopping therapy[28]. Zafirlukast thus offers a potential new treatment for recurrent VVC, however this requires further confirmation in controlled studies.

Alternative therapy

Currently, the available evidence for complementary and alternative therapies for treatment of vaginitis is of poor quality despite the prevalent use of these therapies. Small scale in vitro studies have been done for topical boric acid[29,30], tea tree oil[30], garlic[30], and gentian violet[3]. Well-designed randomised, controlled trials investigating their efficacy and safety of these therapies are needed before any reliable clinical recommendations can be made[30]. Lactobacillus recolonisation seemed to show promise but await further studies[30-32].

Role of Probiotics

In vitro studies have shown that lactobacilli can inhibit the growth of Candida albicans and/or its adherence to the vaginal epithelium[31]. Lactobacillus, especially lactobacillus acidophilus, recolonisation seemed to show promise in the treatment of both candida and bacterial vaginitis with little potential for harm[31,32]. Other than oral administration, there were also small scale studies on yogurt douches in the treatment of bacterial vaginosis[31,32].

Many people practice the use of lactobacillus to prevent post-antibiotic vulvovaginal candidiasis. A randomised, placebo controlled, double blind study on 278 patients, however found no supportive evidence for its use[33].

Other Management Issues

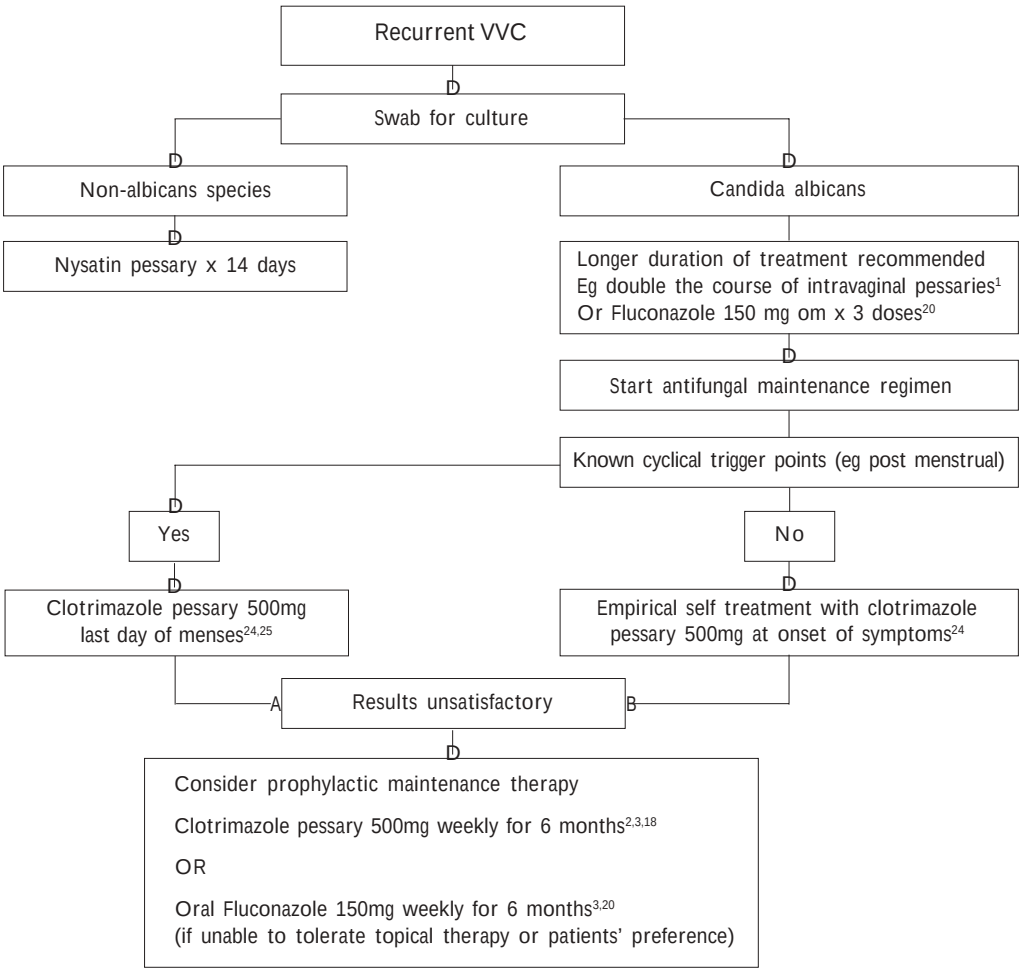
Role of prophylactic antimycotic therapy when using antibiotics

In majority of women who take oral antibiotics, symptomatic vulvovaginal candidiasis does not develop. However, for the patient who has had confirmed antibiotic induced vulvovaginal candidiasis episodes in the past, it is reasonable to prescribe prophylactic antimycotic therapy along with antibiotics[2].

Treatment of sexual partners

VVC is generally not considered a sexually transmitted disease, although it is often associated with initiation of sexual activity[5]. Randomised controlled trials showed no clear evidence that treating the male sexual partner reduced the rate of recurrences of vulvovaginal candidiasis in women[13,34].

Figure 1: Suggested Treatment for Recurrent Vulvovaginal Candidiasis



DISCUSSION

What can we offer women with recurrent vulvovaginal candidiasis?

Recurrent vulvovaginal candidiasis is common and is frustrating to patients. Patients' satisfaction to treatment should be the target for therapy since it is a relatively harmless condition, and relieving the discomfort is the main aim of treatment.

Bearing in mind cost effectiveness and safety profile of drugs, intravaginal antifungal pessary should be the treatment of choice. It is prudent that the side effects of oral antifungal drugs have to be borne in mind in treating a relatively harmless, non-life threatening condition. Only for patients who are not able to tolerate intravaginal antifungal agents due to local irritation, should maintenance oral antifungal drugs be considered. For patients who opt for oral antifungal agents for personal preference, the patient should be adequately informed of its potential side effects of oral antifungal drugs especially if long term usage is required.

It seemed reasonable to give patients a trial of empirical self treatment or monthly clotrimazole pessary before embarking on a weekly maintenance regimen with either oral or intravaginal antifungal agents. Amongst the oral antifungal agents, studies seemed to favour the use of oral fluconazole for treatment of VVC.

Other than antifungal agents, physicians could also help patients with prescription of medications for symptomatic relief. Patients with extensive vulvar inflammation can be treated with low potency topical corticosteroids (e.g. 1% hydrocortisone ointment) to provide immediate relief of vulvar burning, soreness and itch[2,3]. Oral antihistamines can be prescribed at night for relief of intense itch[2,3].

Tips on behavioral practices, though not medically proven, can be attempted since they are harmless and easy to perform. Vulva care measures such as avoidance of harsh soaps or perfumes, the use of 100% cotton undergarments, keeping the genital area dry (moisture can encourage the growth of candida), avoid tight clothing and prolonged use of hot tubs[3] are useful tips for patients. Patients should also be advised to avoid long hours of usage of panty liners, and regular change of sanitary napkins. With regards to dietary changes, consumption of lactobacillus seemed to be of possible though doubtful benefit. Since adverse effects of probiotics are very rare, it seemed reasonable to consider its use especially for women with frequent recurrences[30].

Lastly, family physicians should also deal with the psychosocial impact of the disease. Many women relate vaginal infections to sexually transmitted diseases. This should be dealt with in a sensitive manner.

CONCLUSIONS

Recurrent vulvovaginal candidiasis is defined as four or more episodes a year. A search for predisposing factors is needed and reversible risk factors corrected. Culture is required for confirmation of diagnosis and exclusion of resistant organisms. Non-albicans species should be treated with 14 days of nystatin pessary (Figure 1).

The initial treatment should be adequate with a prolonged course of intravaginal or oral antifungal agents. This should be followed by an antifungal maintenance regimen.

For patients with known cyclical trigger points, e.g. postmenstrual, a maintenance monthly regimen of intravaginal clotrimazole pessary during last day of menses may be helpful. For other individuals with infrequent episodes, empirical self treatment with intravaginal clotrimazole pessary may provide adequate satisfactory results.

For patients who still experience frequent episodes despite the above treatment, prophylactic antifungal maintenance therapy for six months can be initiated. Intravaginal clotrimazole pessary weekly is the regimen of choice. In patients who are unable to tolerate intravaginal agents or prefer oral therapy, oral fluconazole weekly can be used.

Relapse is common after cessation of maintenance therapy. Perhaps, future studies targeting at the immunological component of the disease may provide the answer to treatment of this dreaded disease.

REFERENCES

1. Sheary B, Dayan L. Recurrent vulvovaginal candidiasis. Aust Fam Physician 2005; 34:147-50.
2. Sobel JD, Faro S, Force RW et al.Vulvovaginal candidiasis: epidemiologic, diagnostic, and therapeutic considerations. Am J Obstet Gynecol 1998; 178:203-11.
3. Haefner HK. Current evaluation and management of vulvovaginitis. Clin Obstet Gynecol 1999; 42:184-95.
4. Lanchares JL, Hernandez ML. Recurrent vaginal candidiasis changes in etiopathogenical patterns. Int J Gynaecol Obstet 2000; 71(1 suppl):S29-35.
5. Fidel PL Jr. Immunity in vaginal candidiasis. Curr Opin in Infect Dis 2005; 18:107-11.
6. Moraes PS. Recurrent vaginal candidiasis and allergic rhinitis: a common association. Ann Allergy Asthma Immunol 1998; 81:165-9.
7. Witkin SS, Giraldo P, Linhares I et al. Individual immunity and susceptibility to female genital tract infection. Am J Obstet and Gyneocol 2000; 183: 252-6.
8. Rylander E, Berglund A-L, Krassny C et al. Vulvovaginal candida in a young sexually active population: prevalence and association with oro-genital sex and frequent pain at intercourse. Sex Transm Infect 2004; 80:54-7.
9. Markos AR, Wade AA, Walman M. Oral sex and recurrent vulvo-vaginal candidiasis. Genitouirn Med 1992; 68:61-2.
10. Patel DA, Gillespie B, Sobel JD et al. Risk factors for recurrent vulvovaginal candidiasis in women receiving maintenance antifungal therapy: results of a prospective cohort study. Am J Obstet Gyneocol 2004; 190:644-53.
11. Farage MA, Enane NA, Baldwin RW et al. Labial and vaginal microbiology: effects of extended panty liner use. Infect Dis Obstet Gynecol 1997; 5:252-8.
12. Sobel JD. Management of patients with recurrent vulvovaginal candidiasis. Drugs 2003; 63:1059-66.
13. Ringdahl EN. Treatment of recurrent vulvovaginal candidiasis. Am Fam Physician 2000; 61:3306-12.
14. Nyirjesy P. Chronic vulvovaginal candidiasis. Am Fam Physician 2001; 63:697-702.
15. Review: Oral and intravaginal agents are equally effective for treatment of uncomplicated vulvovaginal candidiasis. ACP Journal Club 2002; v137(1):15. Available at http://gateway.tx.ovid.com. Accessed 2007, Aug 24.
16. Watson MC, Grimshaw JM, Bond CM et al. Oral versus intra-vaginal imidazole and triazole antifungal treatment of uncomplicated vulvovaginal candidiasis (thrush). Cochrane Database of Systematic Reviews 2001;(4): CD002845 (latest version 28 May 2001). Available at http://gateway.tx.ovid.com. Accessed 2007, Aug 24.
17. Reef SE, Levine WC, McNeil MS et al. Treatment options for vulvovaginal candidiasis, 1993. Clin Infect Dis 1995; 20(1 suppl):S80-90.
18. Sobel JD, Brooker D, Stein GE et al. Single oral dose fluconazole compared with conventional clotrimazole topical therapy of candida vaginitis. Am J Obstet Gyneocol 1995; 172:1263-8.
19. Coric M, Barisic D, Lovric H. Fluconazole versus 3-day clotrimazole in the treatment of sporadic and recurrent vulvovaginal candidiasis. Int J Gynaecol Obstet 2006; 95:171-2.
20. Sobel JD, Wiesenfeld HC, Martens M et al. Maintenance fluconazole therapy for recurrent vulvovaginal candidiasis. N Engl J Med 2004; 351:876-83.
21. Sobel JD. Recurrent vulvovaginal candidiasis. A prospective study of the efficacy of maintenance ketoconazole therapy. N Engl J Med 1986; 315:1455-8.
22. Creatsas GC, Charalambidis VM, Zagotzidou EH et al. Chronic or recurrent vaginal candidiasis: short-term treatment and prophylaxis with itraconazole. Clin Ther 1993; 15:662-71.
23. Spinillo A, Colonna L, Piazzi G et al. Managing Recurrent Vulvovaginal Candidiasis. Intermittent prevention with itraconazole. J Reprod Med 1997; 42:83-7.
24. Fong IW. The value of prophylactic (monthly) clotrimazole versus empiric self treatment in recurrent vaginal candidiasis. Genitourin Med 1994; 70:124-6.
25. Lopez-Olmos J, Lerma E. Treatment of recurring vulvovaginal candidiasis: A comparative prospective study during six months of three anti-mycotic preparations of a single dose. Clinica e Investigacion en Ginecologia y Obstetrica 2000; 27:366-75.
26. Fong IW. The value of chronic suppressive therapy with itraconazole versus clotrimazole in women with recurrent vaginal candidiasis. Genitourin Med 1992; 68:374-7.
27. Magliani W, Conti S, Cassone A et al. New immunotherapeutic strategies to control vaginal candidiasis. Trends Mol Med 2002; 8:121-6.
28. White DJ, Vanthuyne A, Wood PM et al. Zafirlukast for severe recurrent vulvovaginal candidiasis: an open label pilot study. Sex Transm Infect 2004; 80:219-22.
29. Guaschino S, De Seta F, Sartore A et al. Efficacy of maintenance therapy with topical boric acid in comparison with oral itraconazole in the treatment of recurrent vulvovaginal candidiasis. Am J Obstet Gyneocol 2001; 184:598-602.
30. Van Kessel K, Assefi N, Marrazzo J et al. Common complementary and alternative therapies for yeast vaginitis and bacterial vaginosis: a systematic review. Obstet Gynecol Surv 2003; 58:351-8.
31. Falagas ME, Betsi GI, Athanasiou S. Probiotics for prevention of recurrent vulvovaginal candidiasis: a review. J Antimicrob Chemother 2006; 58:266-72.
32. Shalev E, Battino S, Weiner E et al. Ingestion of yogurt containing lactobacillus acidophlius compared with pasteurized yogurt as prophylaxis for recurrent candidal vaginitis and bacterial vaginosis. Arch Fam Med 1996; 5:593-6.
33. Pirotta M, Gunn J, Chondros P et al. Effect of lactobacillus in preventing post-antibiotic vulvovaginal candidiasis: a randomized controlled trial. BMJ 2004; 329:548.
34. Fong IW. The value of treating the sexual partners of women with recurrent vaginal candidiasis with ketoconazole. Genitourin Med 1992; 68:174-6.