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Prevalence and management of non-albicans vaginal candidiasis

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ABSTRACT

Objectives It is thought that widespread use of 'over-the-counter' azoles may increase the incidence of resistant *Candida* species such as *Candida glabrata*. Infections with species other than *Candida albicans* frequently do not respond to standard azole treatments. Intravaginal nystatin is an option but is no longer available in the UK. In this paper, the authors review the prevalence of non-albicans candida over the past 5 years, and assess the efficacy of amphotericin and flucytosine vaginal cream in the treatment of non-albicans VVC.

Methods Retrospective review of all vaginal yeast isolates collected from women attending a city centre sexual-health clinic between 2004 and 2008. The women prescribed amphotericin and flucytosine vaginal cream were identified through pharmacy records, and their clinical notes reviewed for treatment outcome.

Results Between 2004 and 2008, the number of isolates of all *Candida* species increased with increasing clinic workload, but the prevalence of non-albicans yeasts remained stable at between 0.87 and 1.06%. Eighteen patients were prescribed amphotericin and flucytosine vaginal cream. At follow-up, all 18 were clear of their initial yeast isolate on culture, but two had persistent symptoms and had positive cultures for *C. albicans*.

Conclusions There is no evidence of any increase in prevalence of non-albicans *Candida* species such as *C. glabrata*. The authors have treated 18 women who had non-albicans VVC with amphotericin and flucytosine vaginal cream and achieved clearance of the non-albicans species in all of them.

INTRODUCTION

The majority of cases of vulvovaginal candidiasis (VVC) are due to *Candida albicans* with other yeasts accounting for about 10%.¹ *Candida glabrata* causes most non-albicans infections.¹ As *C. glabrata* is inherently less susceptible to fluconazole than *C. albicans*, there have been concerns that the widespread use of 'over-the-counter' azoles, particularly fluconazole, might lead to an increase in the incidence of less susceptible *Candida* species such as *C. glabrata*.²⁻³ A previous study suggested this was not the case, but this was published some years ago.²

Non-albicans infections frequently do not respond to standard azole antifungal treatments.³ Intravaginal nystatin is an option, but this treatment became unavailable in the UK during 2007.⁴ Four case reports suggested that amphotericin and flucytosine vaginal cream (amp/flu VC) was an effective treatment for non-albicans VVC,⁵⁻⁶ and this has been used in our clinic since nystatin became unavailable.

In this paper, we review the prevalence of *Candida* species within our clinic over the past 5 years, with particular emphasis on non-albicans species, and assess the efficacy of amp/flu VC in the treatment of VVC caused by non-albicans species.

METHODS

A retrospective review was performed of all vaginal yeast isolates collected from vaginal samples taken from all women with symptoms attending the Leeds Centre for Sexual Health between 2004 and 2008. Positive cultures were quantified and the isolates identified. The germ tube test was used to identify *C. albicans*. All germ tube negative isolates were identified using Auxacolor 2, Dalmau agar and, where necessary, API 32C kits.

The amphotericin 100 mg with flucytosine 1 g in Aquagel per vagina nightly for 14 nights was obtained from the Pharmacy Manufacturing Unit, North Staffordshire Hospital, Stoke-on-Trent. The women prescribed amp/flu VC were identified through the Leeds General Infirmary hospital pharmacy records and their clinical notes reviewed for the outcome of treatment.

RESULTS

The numbers and prevalence of *C. albicans*, *C. glabrata* and other yeasts isolated from the women are shown in table 1.

The number of isolates of non-albicans yeasts has increased, but this is proportionate to the increase in workload of the clinic, and the prevalence has remained stable at between 0.87 and 1.06%. In 2008, there were 31 isolates of *C. glabrata* and 25 isolates of other non-albicans yeasts. Of these, 24 (43%) were asymptomatic at review and so did not require any medication. Eighteen (32%) women had been treated with azoles at their initial visit and did not return for follow-up. Fourteen were treated with amp/flu VC.

During the 2 years from 2006, 18 women were prescribed amp/flu VC. All had had previous episodes of VVC. The yeasts isolated were *C. glabrata* from 15, and one each of *Saccharomyces cerevisiae*, *Candida parapsilosis* and *Candida dubliniensis*. The women had all received clotrimazole or fluconazole initially but remained symptomatic and so were prescribed amp/flu VC. They were followed up 2–4 weeks later with repeat cultures. No significant side effects were reported. At follow-up, all 18 were clear of their initial yeast isolate on culture, but two had persistent symptoms and positive cultures for *C. albicans*. There was partial symptomatic improvement in three women, but some residual vulval irritation remained despite being

Clinical

Table 1 Prevalence of yeasts isolated from women attending the Leeds Centre for Sexual Health between 2004 and 2008

	2004	2005	2006	2007	2008
Total no of cultures	2359	3837	3690	4569	6456
<i>Candida albicans</i>	561	897	880	1141	1756
Prevalence (%) of <i>C albicans</i>	24	23	24	25	27
<i>Candida glabrata</i>	17	29	22	30	31
Prevalence (%) of <i>C glabrata</i>	0.72	0.76	0.60	0.66	0.48
Other yeasts	5	7	17	15	25
Prevalence (%) of other yeasts	0.21	0.18	0.46	0.33	0.39
Total no of non-albicans yeasts	22	36	39	45	56
Prevalence (%) of all non-albicans yeasts	0.93	0.94	1.06	0.98	0.87
Percentage non-albicans isolates of all yeasts	3.8	3.9	4.2	3.8	3.1
Total no of all yeasts	583	933	919	1186	1812

persistently culture negative. These residual symptoms were attributed to irritant dermatitis and settled with emollients and soap substitutes.

DISCUSSION

It has been suggested that the widespread use of azoles, particularly fluconazole, may lead to a pathogen shift and increase the incidence of resistant *Candida* species such as *C glabrata*.²⁻⁵ However, a previous paper from our clinic showed no increase in the prevalence of non-albicans yeasts between 1993 and 1998.² This study has also shown a stable prevalence of non-albicans yeasts between 2004 and 2008, confirming those findings.

The national guidelines for the treatment of VVC recommend nystatin pessaries for non-albicans yeast infections,⁴ but nystatin is no longer available in the UK. Amphotericin is a fungistatic polyene active against many fungi. Flucytosine is a fluorinated pyrimidine antifungal agent that is fungicidal but with a low genetic barrier for resistance. When combined together, they act synergistically with amphotericin B enhancing cellular penetration of flucytosine and thereby potentiating the activity of flucytosine. In addition, if resistance develops to flucytosine, the amphotericin B has activity against the yeasts.

On the basis of successful case reports using amp/flu VC,⁵⁻⁶ we introduced it for the treatment of non-albicans VVC. The treatment is well tolerated but is considerably more expensive than nystatin. The cost of amp/flu VC is approximately £206 per course, compared with nystatin at approximately £10 per

Key messages

- ▶ It has been thought that widespread use of 'over-the-counter' azoles may increase the incidence of resistant *Candida* species such as *C glabrata*.
- ▶ Between 2004 and 2008, the prevalence of non-albicans yeasts remained stable, with no increase in non-albicans *Candida* species such as *C glabrata*.
- ▶ Infections with species other than *C albicans* frequently do not respond to standard azole treatments.
- ▶ Treatment of 18 women with non-albicans VVC using amphotericin and flucytosine vaginal cream achieved clearance of the non-albicans species in all of them.

course. Also, as the shelf-life is unknown, the treatment needs to be started within 48 h of manufacture. The duration of the intravaginal treatment is 14 days and ideally should be avoided during menstruation. Consequently, the ordering and delivery requires coordination with the woman's menstrual cycle to ensure it can be started within 48 h of manufacture at a time when menstruation is not expected for at least 14 days. However, we have now successfully treated 18 women with non-albicans VVC using amp/flu VC with 100% clearance of the non-albicans yeasts.

Competing interests None.

Contributors NH collected the patient data. HRA collected the mycology data and supervised the laboratory testing. HRA and JDW initiated the project. NH and JDW analysed the data. All authors contributed to the preparation of the manuscript.

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REFERENCES

1. **Holland J**, Young ML, Lee O, *et al*. Vulvovaginal carriage of yeasts other than *Candida albicans*. *Sex Transm Infect* 2003;**79**:249–50.
2. **Walker PP**, Reynolds MT, Ashbee HR, *et al*. Vaginal yeasts in the era of 'over the counter' antifungals. *Sex Transm Infect* 2000;**76**:437–8.
3. **Fidel PL**, Vazquez JA, Sobel JD. *Candida glabrata*: review of epidemiology, pathogenesis and clinical disease with comparison to *C albicans*. *Clin Microbiol Rev* 1999;**12**:80–96.
4. *National guideline on the management of vulvovaginal candidiasis*. Clinical Effectiveness Group, British Association of Sexual Health and HIV, 2007. <http://www.bashh.org/guidelines>.
5. **White DJ**, Habib AR, Vanthuyne A, *et al*. Combined topical flucytosine and amphotericin B for refractory vaginal *Candida glabrata* infections. *Sex Transm Infect* 2001;**77**:212–3.
6. **Shann S**, Wilson J. Treatment of *Candida glabrata* using topical amphotericin B and flucytosine. *Sex Transm Infect* 2003;**79**:265–6.