Comparison of miconazole-coated tampons with clotrimazole vaginal tablets in the treatment of vaginal candidosis

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SUMMARY The effectiveness and acceptability of miconazole-coated tampons were compared with those of clotrimazole vaginal tablets in the treatment of vaginal candidosis in 100 women. Both treatments were highly effective in reducing the signs and symptoms of infection; 95% of the group treated with miconazole had negative culture results for *Candida* species immediately after treatment compared with 86% of those treated with clotrimazole. A 17.6% recurrence rate of positive culture results was found four weeks later in the miconazole-treated group compared with that of 30% in the clotrimazole-treated group. The miconazole tampons were highly acceptable to patients. Vaginal pH values did not differ significantly between those patients with candidosis and those treated and cured. *Corynebacterium vaginale* (*Gardnerella vaginalis*) vaginitis and non-specific genital infection were common complicating factors during follow up.

Introduction

Miconazole-coated tampons (Gyno-Daktarin tampons, Janssen Pharmaceutical Ltd) have recently become available in Britain for the treatment of vaginal candidosis. An initial multicentre open study using these tampons¹ showed clinical and mycological cure rates which were similar to those reported for miconazole pessaries and clotrimazole tablets.² This study also showed that the coated tampons were highly acceptable to patients, who preferred them to the other forms of treatment in use for vaginal candidosis.

This single-blind randomised trial assessed and compared the therapeutic effectiveness and acceptability to patients of miconazole-coated tampons with those of clotrimazole vaginal tablets in the treatment of vaginal candidosis. This is the first study of miconazole-coated tampons that provides a randomised comparison with clotrimazole.³

Patients and methods

One hundred women with vaginal candidosis were studied. All had vulval pruritus, with or without vaginal discharge, and *Candida* species were present

on microscopy of a Gram-stained vaginal smear. Patients with associated genitourinary infections and those who had used vaginal or oral antifungal treatments within the previous four weeks were excluded.

CLINICAL FEATURES

Clinical signs and symptoms of burning or soreness, pruritus, discharge, vulvitis, and vaginitis (described as absent, mild, moderate, or severe) were recorded at each visit.

LABORATORY DIAGNOSIS

The cervix was exposed with an unlubricated bivalve vaginal speculum. Specimens of vaginal discharge collected from the posterior and lateral fornices were stained by Gram's method, and material collected similarly on a charcoal-treated swab was placed in Stuart's medium for transport to the laboratory the following morning. Gram-stained smears of urethral and cervical secretion and vaginal wet films were examined microscopically to exclude trichomoniasis, *Corynebacterium vaginale* vaginitis, and gonorrhoea; routine cultures were made from these swabs. Vaginal pH was measured by applying indicator paper to the adherent secretions on the upper tip of the withdrawn vaginal speculum. The swabs in transport medium were subcultured in the laboratory on Sabouraud's medium and *Candida* species identified by standard laboratory procedures.

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TREATMENT

Treatment was randomised and blind to the observer. Each patient received either a five-day course of miconazole-coated tampons inserted twice daily or a six-day course of one clotrimazole vaginal tablet inserted daily. The two drugs were enclosed in numbered identical plain packs, each containing an instruction leaflet and a brief questionnaire. A tube of miconazole or clotrimazole cream for external use, as appropriate, was also included.

FOLLOW UP

Patients were asked to return for follow up after 7-10 days and then four weeks later. All clinical, microscopical, and microbiological studies were repeated at each visit. Cure was defined as the absence of *Candida* species from cultures. When treatment had failed, a course of miconazole pessaries (two inserted daily for seven days) was given. The code was broken at the end of the trial.

STATISTICAL ANALYSIS

The statistical methods used were χ^2 tests with Yates's correction where numbers were small. Student's *t* test was used in connection with the vaginal pH measurements.

QUESTIONNAIRE

The brief questionnaire to assess the acceptability to the patient, which was included with the treatment pack, was completed independently by the patient and brought to the first follow-up visit; a further, more detailed, questionnaire was then completed by the doctor in the presence of the patient.

Ethical approval for the study was given by the appropriate hospital committee.

Results

The two treatment groups were well matched for demographic data. Ages ranged from 17 to 45 years (median 23 years) in the miconazole-treated group and from 16 to 55 (median 22 years) in the clotrimazole-treated group. One patient in each group was pregnant. Thirty (60%) of the miconazole-treated group and 32 (64%) of the clotrimazole-treated group had a history of previous candidosis; 21 (42%) of the former and 22 (44%) of the latter were taking oral contraceptives.

Except for one patient from India and one from France in the miconazole-treated group, the patients were all of British origin.

CLINICAL SIGNS AND SYMPTOMS

Both treatments were highly effective in reducing the signs and symptoms of vaginal candidosis. Only

three (3.5%) of the 86 patients attending the first follow-up visit had moderate or severe symptoms and signs, and all three had positive culture results for *Candida* species. Of these, two had been given clotrimazole tablets and one miconazole-coated tampons.

CULTURES

Of the 100 patients entered in the trial, 98 had positive culture results for *Candida* species; of these, 86 (87.8%) were available for study at the first follow up (table I). In the miconazole-treated group 41 (95.3%) of 43 patients had negative culture results at the first follow-up visit. For the clotrimazole-treated group the apparent cure rate was 86% (37/43).

TABLE I Results of treatment using miconazole-coated tampons and clotrimazole tablets

Treatment	Culture results for <i>Candida</i> species at:							
	First visit (n = 86)				Final visit (n = 64)			
	Negative		Positive		Negative		Positive	
	No	%	No	%	No	%	No	%
Miconazole-coated tampons	41	95.3	2	4.7	28	82.4	6	17.6
Clotrimazole tablets	37	86.0	6	14.0	21	70.0	9	30.0
Total	78	90.7	8	9.3	49	76.6	15	23.4

RECURRENCE RATE

Candidosis was considered to have recurred in those patients with positive culture results at the final visit after previous apparent cure. The recurrence rate was 17.6% (6/34) in the miconazole-treated group and 30% (9/30) in the clotrimazole-treated group (table I). These differences in the apparent cure and recurrence rates are not statistically significant.

VAGINAL pH

The vaginal pH measurements did not differ significantly between those patients with and without candidosis; 98 patients with candidosis had a mean vaginal pH of 4.7 (SD ± 0.3), and 74 uninfected patients at first follow up and 53 at final follow up had a mean vaginal pH of 4.6 (SD ± 0.3).

OTHER DIAGNOSES

Four patients (4.7%) had *C. vaginale* vaginitis with negative culture results for *Candida* species at the first follow up visit. They were cured with a five-day course of metronidazole 400 mg twice daily; in one patient candidosis had recurred again at her final visit. At the final visit a further three patients had *C. vaginale* vaginitis (two of these also had positive

culture results for *Candida* species) and one patient had trichomoniasis, one gonorrhoea, and three non-specific genital infection.

ACCEPTABILITY OF TREATMENT

Of the 62 patients who had had previous treatment for vaginal candidosis 51 (82.3%) completed the questionnaires. In the miconazole-treated group 19 (66%) of 29 rated miconazole tampons as better or very much better than any previous treatment, whereas only seven (32%) of 22 of the clotrimazole-treated group gave a similar rating. This difference is statistically significant ($P<0.05$).

When asked about the best or worst features of treatment, patients receiving miconazole tampons clearly regarded convenience and lack of mess as the best features. In the clotrimazole-treated group convenience was the most often selected best feature but a large majority considered messiness to be the worst. No particularly bad feature was identified by the patients in the miconazole-treated group. When asked to comment on the degree of messiness (as judged by the need for protective wear or a change of underwear), 77.3% (34/44) of the patients in the clotrimazole-treated group considered the treatment to be slightly or very messy, whereas 17.4% (8/46) found the miconazole tampons slightly messy, although none found them very messy. This difference is highly significant ($P<0.0001$). More detailed analysis of the questionnaires will be presented elsewhere.

SIDE EFFECTS

There were no serious adverse effects resulting from either regimen. Four patients in each group mentioned mild burning or irritation in the first few days of therapy.

Discussion

Infection with *Candida* species is the most common cause of vaginitis, is often recurrent, and appears to be increasing in incidence. Intravaginal antifungal therapy in the form of pessaries, tablets, and cream has always been unpopular with patients because of leakage of medication from the vagina,^{4,5} particularly when treatment continues for many days. Because of this, patients may discontinue treatment and fail to attend for follow up.⁶ The introduction of a five-day course of miconazole-coated tampons now offers a convenient and acceptable alternative.

The cure and recurrence rates in this trial are comparable with results recently published separately for miconazole-coated tampons¹ and clotrimazole vaginal tablets² (table II). The results for miconazole tampons compared favourably with those for miconazole pessaries and cream.^{7,8} The cure rates

immediately after treatment were similar for the groups treated with miconazole-coated tampons and clotrimazole tablets. The recurrence rates, however, were lower in the miconazole-treated group but not significantly so in the present study.

TABLE II Comparison of cure and recurrence rates in three recent studies

Study	Treatment	No of patients treated	Cure rate* (%)	Recurrence rate† (%)
Eliot <i>et al</i> ²	Clotrimazole vaginal tablets	60	88.7	28.3
Rosedale <i>et al</i> ¹	Miconazole-coated tampons	195	88.5	12.1
Balsdon (present study)	Clotrimazole vaginal tablets	50	86.0	30.0
	Miconazole-coated tampons	50	95.3	17.6

*Negative culture results for *Candida* species at first follow-up visit.

†Cured at the first follow-up visit but positive culture results at second follow-up visit.

Vaginal pH values did not differ significantly during or after vaginal candidal infection. Conflicting and confusing results,^{9,10} often due to a few high pH values, can possibly be explained by the inclusion in the data of patients with conditions such as *C. vaginale* vaginitis, in which pH values are invariably 5.3 and above.¹¹ The great majority of patients with vaginal candidosis have vaginal pH values in the normal range of 4.2-5.0 (unpublished data).

Seven patients developed *C. vaginale* vaginitis during the trial. Until recently this condition has not often been diagnosed in Britain.¹¹ Its presence may account for a proportion of those patients with candidosis who are apparently cured but still have discharge and irritation. Davidson and Mould¹² found a high incidence of non-specific genital infection in their group of patients with candidosis. Non-specific genital infection and *C. vaginale* vaginitis were also found in patients followed up during this study.

The miconazole-coated tampons were highly acceptable to patients, as treatment lasts for only five days and there is no leakage of medication from the vagina. This latter aspect was regarded by most patients as the best feature of miconazole-coated tampons and the worst feature of clotrimazole vaginal tablets. A further advantage of tampons is that most women are accustomed to using them routinely during menstruation. Several women commented that they always used menstrual tampons to avoid the leakage from vaginal pessaries and creams. Miconazole-coated tampons thus provide a valuable contribution to the management of a common, recurrent, and troublesome condition.

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