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Clotrimazole and econazole in the treatment of vaginal candidosis

A single-blind comparison

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SUMMARY Clotrimazole and econazole used as treatment for vaginal candidosis are both effective when given for three days. In a single-blind controlled study of 110 women followed for 14 days the efficacy of treatment with clotrimazole and econazole for three days was equal. Eighty-six per cent of the group treated with clotrimazole were mycologically clear at 14 days compared with 90% of those treated with econazole. Both treatment regimens were equally acceptable to the patients and no side effects were reported.

Introduction

For many years vaginal candidosis was treated with intravaginal antifungal agents for about two weeks. Recently, the newer antifungal drugs have been used successfully over shorter periods of time. Masterton *et al*[1] noted that many of their patients failed to complete a six-day course of clotrimazole treatment; they demonstrated the efficacy of clotrimazole over a three-day period.

Econazole is another antifungal agent which has been found to be effective when used for three days.[2,3] We have carried out a single-blind comparison of the efficacy of these two antifungal agents in the treatment of vaginal candidosis.

Patients and methods

All women attending the department of genital medicine at St Bartholomew's Hospital, London, with symptoms and signs suggesting vaginal candidosis were considered for entry into the study. Patients who were taking long-term tetracycline and those who had been treated in the preceding two weeks for candidosis were not included. Patients were included in the study by the following criteria: a minimum of one symptom or sign must have been present; microscopy of a Gram-stained smear must have shown pseudohyphae or spores; and subsequent culture for *Candida albicans* must have been positive. Using a cottonwool swab specimens were taken from the upper vagina, a smear was made on a slide, and Sabouraud's medium was inoculated for subsequent identification of *C albicans* in the laboratory. The smear was stained by Gram's method and read microscopically by experienced clinic nurses. In the laboratory the media were examined after 48 hours and then discarded. In all patients wet preparations of vaginal secretion were also examined microscopically for the presence of *Trichomonas vaginalis* and secretions were inoculated into *T vaginalis* culture medium (prepared by Medical Wire Co Ltd). In the case of new patients or patients who had not attended the department during the previous three months, or where indicated for other reasons, the appropriate specimens were taken to diagnose or exclude gonococcal infection.

Once the doctor had entered the patient into the trial treatment was given by the clinic nurse in a separate treatment room. Using a random numbered sequence patients were given either one 200-mg clotrimazole pessary at night for three consecutive nights or one 150-mg econazole pessary at night for three consecutive nights. Each patient was given a numbered, but otherwise identical, treatment pack; each contained three pessaries and a tube of cream. Although the clotrimazole and econazole pessaries were not identical, they were identically wrapped in unlabelled aluminium foil. Patients were instructed to insert one pessary each night for three consecutive nights. If there was no clinical indication for cream, the tube was removed from the pack by the clinic nurse and kept. If clinically indicated, the patient was advised to apply the cream twice a day after saline washing.

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The patients were asked to re-attend 14 days and 28 days after the start of treatment. At these attendances Gram-stained smears of secretions from the vaginal fornix were examined microscopically; secretions were also inoculated into Sabouraud's medium. There was no indication in the case notes as to which of the two treatment regimens had been prescribed and none of the doctors knew which treatment had been dispensed by the nursing staff. Any concomitant condition was treated in the usual way.

Any patient with treatment failure was given two nystatin pessaries at night for 14 consecutive nights. Patients were advised that any sexual partner with whom they were likely to have contact again should attend the clinic. They were treated with the same cream as the patient and again the doctors were unaware of the type.

Results

A total of 156 patients was studied; *C albicans* was the only fungus isolated from vaginal secretions. Seventy-seven women were treated with econazole and 79 with clotrimazole (table I). Of the econazole group, 32 were treated with pessaries alone and 45 with pessaries and cream. In the clotrimazole group 30 were treated with pessaries alone and 49 with pessaries and cream.

TABLE I *Clinical and laboratory findings before treatment of women with candidosis*

	No of women with:			
Treatment	*Symptoms*	*Signs*	*Positive Gram-stain smears*	*Positive cultures*
Clotrimazole	71	53	33	79
Econazole	69	49	36	77

In the econazole group the women's ages ranged from 17 to 45 years with a mean of 25·4 years. Sixty-six patients in this group were from Britain, four from the rest of Europe, two from the West Indies, and five from outside these areas. In the clotrimazole group 62 originated from Britain, nine from the rest of Europe, two from the West Indies, and six from outside these areas.

Data on marital state, parity, and contraceptive methods used are compared in table II.

TABLE II *Data on marital state, parity, and contraceptive methods used for patients in the two treatment groups*

	Treatment group	
	Econazole	*Clotrimazole*
Marital state:		
Single	57	59
Married	13	11
Previously married	7	9
Parity:		
Nulliparous	62	59
One pregnancy	9	14
Two or more pregnancies	6	6
Contraceptive methods used:		
Oral (%)	48	51
None (%)	18	19
Barrier (%)	15	17
Intrauterine device (%)	15	12
Other	4	0

TABLE III *Results of mycological examination of vaginal material from women treated for candidosis*

	No of women:			
Treatment	*Treated*	*Defaulted*	*Followed for 14 days*	*With no evidence of fungal infection 14 days after treatment (%)*
Clotrimazole	79	19	60	52(86·6)
Econazole	77	22	50	45(90·0)

MYCOLOGICAL RESPONSE

The overall results for the two groups are shown in table III. There was a relatively high rate of default at the two-week follow-up stage in both groups. Of the clotrimazole group, 60 patients were followed for 14 days and 52 (86·6%) had no evidence of fungal infection. In the econazole group there was a slightly higher rate of default and 50 patients were followed for 14 days; 45 (90%) women had no evidence of candidosis. Of the eight failures in the clotrimazole group three patients reported a noticeable improvement in their symptoms. In the econazole-treated group, of the five failures, two were symptom-free after treatment though *C albicans* was found on microscopy and culture. Unfortunately, the default rate at 28 days was very high in both groups, with 78% of patients in the clotrimazole and 75% in the econazole treated group failing to attend.

SYMPTOMATIC RESPONSE

Symptomatic and clinical response was assessed in patients who had no mycological evidence of infection at 14 days (table IV). All signs resolved in both

TABLE IV *Symptomatic response of patients treated for vaginal candidosis with clotrimazole or econazole*

	No of women:	
	Symptomatic before treatment	*Symptom-free after treatment (%)†*
Clotrimazole	46	45(97)*
Econazole	37	33(89)*

*No significant difference (χ_2 analysis)
†After treatment *C albicans* was not isolated from the vagina of any patient

treatment groups. With the exception of one patient in the clotrimazole-treated group who found difficulty in inserting the pessaries, with consequent treatment failure, no patients reported any side effects. All other patients found the treatment acceptable.

Conclusion

While this was not a double-blind comparative trial it was single blind and the laboratory was unaware of the treatment given when the post-treatment cultures were read. We believe that with the identical packaging and randomisation it is reasonable to compare the findings in these two groups of patients. Both treatments gave similar clinical and mycological results, both were acceptable to the patients, and both were free from side effects. Probably the clinician should choose between the two on the basis of cost and availability.

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