

## Comparison of econazole and isoconazole as single dose treatment for vaginal candidosis

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**SUMMARY** In a single blind trial there was no significant difference between econazole (2 × 150 mg pessaries) and isoconazole (2 × 300 mg pessaries) given as a once only treatment for vaginal candidosis. Cure rates at 14 days were 70·4% for econazole and 77·6% for isoconazole, and at 28 days were 63·8% and 64·5% respectively.

Though isoconazole was formulated for single dose usage, econazole was formulated for a regimen of one pessary a night for three nights.

### Introduction

The incidence of candidosis reported from sexually transmitted disease (STD) clinics in the United Kingdom is rising,<sup>1</sup> and at a time when pressures for economy are increasing it is important to examine treatment regimens. There is a trend towards the use of shorter courses of all antimicrobial treatment,<sup>2</sup> and new imidazole derivatives, such as isoconazole, seem to provide treatment for vaginal candidosis in single dosage. If this is effective it is simpler for the patient and should improve compliance and reduce costs. We therefore undertook a single blind trial comparing econazole (Ecostatin; Squibb, Hounslow, England) with isoconazole (Travogyn; Berlimed, Burgess Hill, England) each given in a single dose of two pessaries.

### Patients and methods

#### PATIENTS

Patients attending the STD clinic at this hospital were included if they had signs or symptoms, or both, of vaginal candidosis (such as vaginal discharge, itch, swelling, or fissuring), a positive culture of vaginal secretion for yeasts, and were prepared to attend for follow up after treatment. They were required to give informed consent.

Patients were excluded from participation if they were currently receiving broad spectrum antibiotics or

if they had used antifungal medication in the preceding 28 days.

#### METHODS

Patients were seen routinely in the clinic by a duty doctor. After the history had been taken and physical examination performed, a bivalve speculum was inserted and the vagina inspected. Secretion was collected from the vaginal walls for Gram staining and immediate microscopy for yeasts or any clue cells<sup>3</sup> and another sample was plated on to Sabouraud's medium for culture for yeasts. In addition, vaginal secretion was collected from the posterior fornix, mixed with physiological saline, and examined microscopically for clue cells<sup>3</sup> and *Trichomonas vaginalis*. Another sample of secretion from the posterior fornix was inoculated into Feinberg's medium. The Sabouraud's and Feinberg's media were incubated at 37°C in 10% carbon dioxide and examined after 48 hours.

All patients were investigated for other STDs as follows.

We took blood samples for the Venereal Disease Research Laboratory (VDRL) test and the *Treponema pallidum* haemagglutination assay (TPHA), and undertook additional fluorescent treponemal antibody-absorbed (FTA-ABS) investigation when any positive results were obtained or there was any suggestion of treponemal disease.

We collected material for the isolation of *Neisseria gonorrhoeae* from the urethra and cervix of all patients, and from the rectum and pharynx of sexual contacts of patients with gonorrhoea. This material was then used to make Gram stained slides, and was plated on to modified Thayer-Martin medium.<sup>4</sup>

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Accepted for publication 12 April 1985

We collected secretions for chlamydia culture from the cervical os with cotton tipped, wire mounted swabs, which were cut off into 2 ml Eagle's minimum essential medium containing 10% fetal serum, 5% glucose, and gentamicin 10 g/l plus vancomycin 10 g/l. Specimens were transferred to the laboratory in two to 10 hours, where they were inoculated the same day by the method described by Reeve *et al*<sup>5</sup> on to monolayers of iodouridine treated McCoy cells and incubated at 37°C for 48-72 hours. The cells were then stained with Lugol's iodine, and chlamydiae were identified by finding typical inclusion bodies.

We took cultures for herpes simplex virus from all ulcers, and specimens were inoculated into virus transport medium and thence on to confluent monolayers of VERO cells and lung fibroblasts. Specimens were incubated at 37°C for seven days. The virus was recognised by the typical cytopathic effect. We also collected scrapings for dark ground microscopic investigation.

TREATMENT

We prescribed treatment on the basis of the clinical features and vaginal secretion from Gram stained findings, but patients were only included in the trial if the culture gave a positive result. Each patient was instructed in the insertion of pessaries, and was asked to return after 14, 28, and 84 days. Sexual intercourse was not prohibited. Two intravaginal pessaries were inserted on the evening of the first visit. The dose of isoconazole was 600 mg and of econazole 300 mg. Both drugs were packed in identical numbered boxes (by Squibb) according to a random number table.

Patients whose vulvas were affected were also prescribed clotrimazole or nystatin cream.

At each follow up visit, vaginal secretion was collected as above for immediate examination and culture. Any patient failing to return for the first follow up was sent one reminder letter.

The study was approved by the ethical committee of this hospital.

Results

We studied 196 patients; 99 received econazole and 97 isoconazole. Table I shows that they were well matched for age, race, number taking oral contraceptives, and history of candidosis. More patients receiving isoconazole were diabetic or were pregnant, and more patients receiving econazole had received antibiotics in the preceeding month. We gave 36 patients antifungal cream in addition to the pessaries. Seventeen patients receiving isoconazole and 21 receiving econazole failed to attend for any follow up, two attended after an interval of two months or more and were therefore excluded from the analysis, and four were withdrawn after receiving further antifungal treatment from their general practitioner for symptomatic relapse. Thus 152 patients remained for analysis.

Five patients given isoconazole but only two given econazole complained of irritation after the insertion of their pessaries. One patient from each treatment group said the pessaries had failed to disperse. Table II shows that 103 patients attended for the first follow up visit and, partly because of reminder letters, a further 49 attended within 28 days of treatment thus totalling 152 (77.6% of all 196 patients studied). The cure rates for econazole were 70.4% at 14 days and 63.2% at 28 days whereas the figures for isoconazole were 77.6%

TABLE I. Comparison of treatment groups of women with vaginal candidosis. Figures are numbers of patients except where stated.

	Econazole (n = 99)	Isoconazole (n = 97)	Difference
Mean age (years)	25.8	25.0	
Racial origin:			
White	52	56	
Black	46	40	
Other	1	1	
Using oral contraceptives	47	44	
Received antibiotics in month before entry	37	24	$\chi^2 = 4; 0.5 > p > 0.025$
Attack of candidosis in preceeding 6 months	30	30	
Diabetic	0	3	} $\chi^2 = 0.14$ (NS)
Pregnant	1	6	
Concurrent prescription of antifungal cream	22	17	

TABLE II. Cure rates of vaginal candidosis in women treated with econazole compared with isoconazole.

	Econazole	Isoconazole	Difference
No seen by day 14	54	49	
No (%) cured at day 14	38 (70.4%)	38 (77.6%)	$\chi^2 = 0.79$ (NS)
Total seen by day 28	76	76	
No (%) cured at day 28	48 (63.2%)	49 (64.5%)	$\chi^2 = 0.2$ (NS)
No treated by GPs	4	0	

and 64.5% respectively. There was no significant difference between these results.

### Discussion

Both drugs were shown to be effective in the treatment of vaginal candidosis. The cure rate at 14 days may in reality have been higher owing to the poor follow up and possible bias in favour of symptomatic patients.

Our results were better than those of Velupillai and Thin,<sup>6</sup> but inclusion of high risk groups of patients, such as diabetics and pregnant women, may have lowered our cure rates compared with those of other trials.<sup>7-8</sup> Our range of patients may be more similar to those treated in clinical practice than those selected for some trials.

The effectiveness of the two drugs did not differ, but econazole was given in half the dosage of isoconazole and may cause less irritation. Furthermore, isoconazole was formulated for single dose usage, whereas the econazole pessaries were formulated for insertion one a night for three nights.

Single dosage is especially useful for the treatment of candidosis in patients with minimum symptoms, in whom compliance may be poor, and also in asymptomatic patients who are to receive antibiotic treatment. Single dosage also has the advantage of economy, which is important when efforts are being made to reduce prescribing costs.

We thank E R Squibb and Sons Limited for the supply of econazole, and Berlimed for the supply of isoconazole. Dr D Chalmers of E R Squibb and Sons Limited kindly arranged the randomisation.

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