A clinical study of econazole cream in the treatment of fungal skin infections

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SUMMARY. An open assessment of the efficacy of econazole nitrate (Pevaryl) cream in the treatment of 140 patients with proven dermatomycoses was conducted at five university health centres. Specimens were obtained from 129 patients at the end of treatment and 121 (93.8 per cent) showed no evidence of fungi. After a further month without treatment 108 patients reattended and, of these, 98 (90.9 per cent) remained clinically and mycologically free from infection. *Trichophyton rubrum* and *Epidermophyton floccosum* were the fungi most frequently isolated, and the distribution of species and areas of the body affected were similar for all five centres.

Introduction

ECONAZOLE nitrate has been shown to possess significant antifungal activity *in vitro* (Dorn *et al.*, 1975), and a high degree of penetration is achieved following application to the skin (Schaefer and Stuttgen, 1976). As a result of studies carried out in mainland Europe, it has been described as the drug of choice in the management of fungal skin infections (Raab, 1977). It was decided, therefore, to assess its value in the treatment of the superficial mycoses occurring in the United Kingdom.

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Methods

Five university health centres participated in the study: Birmingham, Loughborough, Manchester, Lancaster and Edinburgh. By using more than one centre to recruit patients, a large number were enrolled and it was thought that this method would provide some indication of the prevalence of fungal species, the sites infected and the geographical distribution within the United Kingdom.

Materials and methods

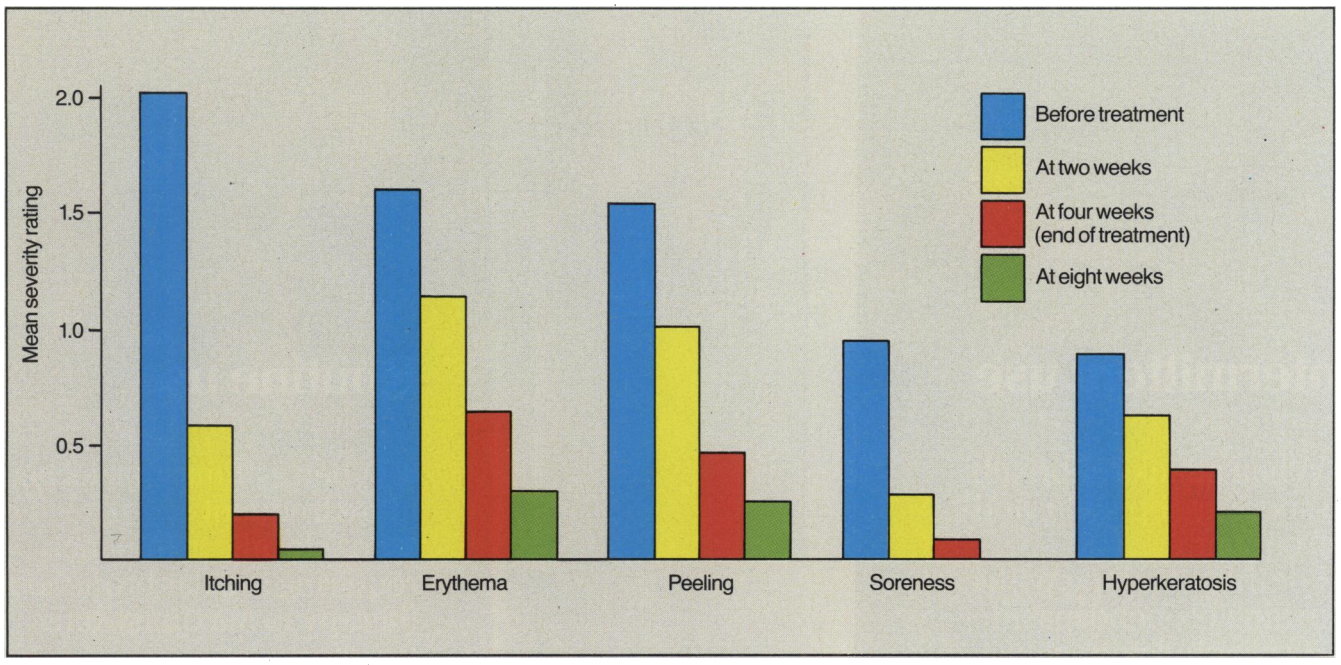
Patients were enrolled in the study on the basis of a clinical diagnosis of fungal skin infection. A clinical assessment was carried out and the severity of presenting symptoms was recorded on a scale from 0 (no symptoms) to 3 (severe). Patients were requested to apply 1% econazole nitrate (Pevaryl) cream twice daily to the affected area for approximately 28 days and to return for assessment about three or four days after stopping treatment. Whenever possible, patients were also seen about two weeks after their treatment began for an interim clinical evaluation. In addition, patients were asked to return for a follow-up appointment at least one month after therapy had been completed to assess the incidence of relapse or reinfection (that is, where the species isolated at the start of the study had been replaced by a different fungus).

Mycology

Skin specimens were collected as vinyl adhesive tape strippings (Milne and Barnetson, 1971) at the first visit, after completion of the course of treatment and again at the follow-up visit one month later. Uniform standards of diagnosis were maintained by carrying out all mycological assessments at a single centre. All specimens were sent to the Mycology Unit, Western General Hospital, Edinburgh, for culture of the causal organism except in cases of suspected pityriasis versicolor, when direct microscopy was substituted. Only patients in

Table 1. Mycology results after treatment.

Mycology	End of therapy (four weeks) Patients (n=129)	Per cent *(100.0)*	Follow-up (eight weeks) Patients (n=108)	Per cent *(100.0)*
Negative	121	*93.8*	98	*90.7*
Positive (same species as pre-treatment)	3	*2.3*	5	*4.65*
Positive (different species from pre-treatment)	5	*3.9*	5	*4.65*



Signs and symptoms in relation to econazole therapy.

whom the clinical diagnosis was confirmed by mycological examination were retained in the study and their data analysed.

Results

Two hundred and fifty-one patients were entered into the study, but in only 140 (55.8 per cent) was it possible to demonstrate a fungus in the specimen of skin submitted for laboratory examination. After one month of therapy 129 patients with a mycologically confirmed diagnosis returned for assessment and 121 (93.8 per cent) were found to be free from infection (see Table 1). At follow-up one month after completion of treatment, 108 patients reattended and 98 (90.7 per cent) remained clinically and mycologically cured.

Clinical response to treatment is demonstrable by the reduction in the mean value accorded to the severity of symptoms (see Figure). The average time taken for symptoms to disappear by subjective assessment was seven days. No side-effects were detected and patients frequently commented upon the acceptability of the medication.

Table 2 shows the incidence of species isolated for the five centres. The most common species were *Trichophyton rubrum* and *Epidermophyton floccosum,* there being no significant geographical variation in their distribution. Similarly, there was no marked difference between centres in respect of the sites affected by fungi (see Table 3). The groin was the most common site for the manifestation of infection, followed by the foot.

Discussion

This study confirms the difficulty of making a firm diagnosis of superficial mycosis on clinical grounds alone, as no fungi were found in specimens collected from almost half the suspected cases. Where mycological evidence was obtained, there was generally a rapid (seven days) response to topical 1% econazole nitrate cream and no side-effects were noted. Treatment twice daily for four weeks produced a cure rate of 93.8 per cent and at follow-up one month after stopping therapy 90.7 per cent remained clinically and mycologically free from infection.

Table 2. Geographical distribution of species (includes mixed cultures and reinfections).

Organism	Total for all centres	Percentage of total for each centre				
		Birmingham	Loughborough	Manchester	Lancaster	Edinburgh
Trichophyton rubrum	59	*44.2*	*40*	*34.3*	*33.3*	*37.5*
Epidermophyton floccosum	30	*13.5*	*20*	*28.6*	*11.1*	*22.5*
Candida albicans	24	*17.3*	*20*	*14.3*	*44.5*	*7.5*
T. mentagrophytes	18	*9.6*	*20*	*8.6*	*11.1*	*15.0*
Malassezia furfur	12	*7.7*	—	*11.4*	—	*10.0*
T. verrucosum	5	*7.7*	—	—	—	*2.5*
Microsporum canis	2	—	—	*2.8*	—	*2.5*
T. tonsurans	1	—	—	—	—	*2.5*
Total		*100*	*100*	*100*	*100*	*100*

Table 3. Geographical distribution of body sites infected with fungi.

Site	Total for all centres	Percentage of total for each centre				
		Birmingham	Loughborough	Manchester	Lancaster	Edinburgh
Groin	69	*44.8*	*53.8*	*63.6*	*55.5*	*40.5*
Foot	52	*39.7*	*46.2*	*21.3*	*44.5*	*43.3*
Trunk						
Pityriasis versicolor	12	*8.3*	—	*12.1*	—	*10.8*
Other fungi	3	*2.0*	—	*3.0*	—	*2.7*
Face	3	*4.2*	—	—	—	*2.7*
Scalp	1	*2.0*	—	—	—	—
Total		*100*	*100*	*100*	*100*	*100*

The results reported are comparable to those from Germany (Scherwitz, 1977) and France (Pastel *et al.*, 1976), where cure rates of 87.3 and 91 per cent respectively were obtained. However, in a series of 33 patients, two Danish workers (Stahl and Onsbert, 1978) found that only 66 per cent of their patients were cured after treatment twice daily for one month with econazole. The reasons for this discrepancy are unclear.

In our hands, 1% econazole nitrate cream has proved to be a safe, effective treatment for superficial mycoses, irrespective of the causal fungus. It is noteworthy that some of our patients who responded well had long-standing infections, in some instances of at least 10 years.

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Acknowledgements

The authors wish to thank Ortho Pharmaceutical Limited for supplying the 1% econazole nitrate (Pevaryl) cream used in this study. The support of many associates in administrative and technical capacities is gratefully acknowledged.

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