

Tinea versicolor treated with a whole-body foaming solution

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Summary

Tinea versicolor is the commonest superficial fungal disease in tropical and sub-tropical regions. The aetiological agent is P. orbiculare, a normal skin-commensal which, under certain conditions, not all of which are understood, alters morphology and becomes invasive, producing the disease tinea versicolor. In this double-blind study on 100 patients, econazole, in the form of a whole-body, shampoo-like foaming solution, and a placebo foaming solution were used for three applications. As judged clinically, by Wood's light for fluorescence and on microscopy, the econazole foaming solution was statistically superior at the level of ($p < 0,001$) in clearing both the mycelial forms of P. orbiculare and the skin disorder. Three years after the original application 25% of the patients are still clinically clear of a skin condition notorious for its tendency to relapse after a wide variety of treatment modalities. The authors feel that this foaming solution form of econazole is a useful addition to the tropical

practitioner's armamentarium, particularly if the initial treatment phase is followed by regular applications once a month. The preparation was totally free from side-effects and was cosmetically acceptable.

KEYWORDS: Tinea Versicolor; Physicians, Family; Disease Susceptibility; Recurrence; Patient Acceptance of Health Care; Prescriptions, Drug.

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Tinea versicolor is the commonest superficial mycotic disease seen in tropic and subtropic regions. In our family practice in Durban the incidence of the condition in patients between the ages of 15 and 50 years ranges from 15% in the cooler months to over 35% during the period November to March. Apart from pruritus the disorder is usually asymptomatic but presents as disfiguring hyperpigmented or hypopigmented scaly patches affecting the arms and trunk. (See fig 1).

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Clinical picture of *T. versicolor*.

Pityrosporum orbiculare, the dimorphic fungus and causative agent of tinea versicolor, was first isolated in the early fifties.¹ It is an ubiquitous fungus which should probably be regarded as a normal skin commensal as it can be cultured from the normal skin of over 90% of all adults.² Under certain conditions, not all of which are understood, the organism, which in its dormant state appears as roundish spores, undergoes mycelial conversion and becomes invasive and burrows into the upper two-thirds of the horny layer, causing the disease tinea versicolor. It has now become customary to refer to the organism in its invasive mycelial form by its original name, *Malassezia furfur*. (See fig II).



Microscopic view of Mycelia of *P. orbiculare*. Scrapings from Active lesions stained with Parker ink/KOH and examined immediately.

A large number of topical modalities induce a temporary improvement of apparent clearing of the tinea lesions, but the number of treatments tried is an indication of the lack of success of any one treatment in the long term. The ubiquitous prevalence of the fungus and its tendency to become invasive for no obvious reason have meant that relapses are the rule. Another problem with topical treatment is that some of these have been found to be cosmetically unacceptable or irritant. Selenium sulphide ("selsun") has long been considered an inexpensive, safe and effective treatment for tinea versicolor³ but our own experience with extensive and disseminated cases has been that many patients find it causes irritation and burning especially in flexure areas. In one of the few controlled studies on the use of "selsun"⁴ 16% to 18% of patients experienced side-effects with selenium sulphide lotion or with the colouring agent used in the preparation of the shampoo. The topical forms of many imidazole derivatives have also had short-term success but are

also inconvenient in lotion or creme forms where lesions are widespread or inaccessible as on the back. Systemic imidazole derivatives such as ketoconazole⁵ and Itraconazole⁶ have been effective taken systemically. As with the topical imidazoles, however, ketoconazole therapy is also followed by a high incidence of recurrences^{7,8}, and this has led to the suggestion that monthly follow-up doses of the drug be employed.^{9,10} The fact that transient elevations of hepatic enzymes have been found to occur with the use of ketoconazole would cause many to question the long-term use of the drug in a condition with essentially cosmetic effects.

We decided to investigate the effect of the imidazole derivative econazole* in the form of a whole-body foaming solution in a controlled clinical trial in our family practices in the suburbs of Durban during the Summer months.

PATIENTS AND METHODS

There were two phases to the study:

- (1) A double-blind phase, in which, following a parallel group, randomised, double-blind design, patients were treated with either foaming-solution containing econazole base or identical appearing and scented placebo foaming solution.
- (2) An open phase in which non-responders to placebo foaming solution received known econazole base foaming solution.

Tinea Versicolor is caused by a normal skincommensal which, under certain conditions, changes and becomes invasive.

The study included 100 patients with widespread lesions of tinea versicolor which had relapsed after a variety of topical treatments, chiefly "selsun". All patients had involvement of at least 25% of the trunk area. Pregnant women and patients who had been on any antifungal therapy during the month prior to entry were excluded from the study as were any patients with serious concomitant disease. The diagnosis, initially made on clinical grounds, was confirmed by Wood's light examination for the characteristic fluorescence, and by microscopy of scrapings stained by our modification of the Parker Quink/KOH method¹¹ in which we diluted equal parts of 30% KOH and Parker permanent blue/black ink and applied a drop to scrapings on a slide which was examined immediately for the blue-stained spores and myceliae. In addition, skin scrapings were cultured, on a peptone/glucose/yeast-extract medium containing glycerol monostearate overlaid with olive oil as described by Faergemann & Bernandes¹².

*Trade name: PEVARYL® Foaming Solution Fisons (Pty) Ltd SA.

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After positive confirmation on microscopy and Wood's light subjects had a three-day overnight treatment with either placebo or econazole-base foaming solution. The preparations had to be used in shampoo fashion on both body as well as hair and allowed to dry without rinsing and showered off next morning. Patients were re-examined (again with microscopy and Wood's light and culture) at intervals of 8, 16, 24 and 32 days. After 32 days the code was broken and all negative responders who had previously received placebo foaming solution were given three applications of econazole base foaming solution and re-examined after a month. Thereafter all patients who were negative on microscopy and Wood's light were followed at monthly intervals until they relapsed. Three patients failed to return for their first follow-up and were not included in the evaluation, leaving 97 patients for assessment, whilst another six (five placebo and one in the econazole group) failed to attend for the last (32 day) visit.

A single application once a month has kept patients clear for 2 years now.

RESULTS DOUBLE-BLIND PHASE

The clinical data on the 97 patients is shown in Table I. The two populations were homogenous with regard to age, sex and severity and duration of disease. Five patients, two in the placebo group and one in the econazole group, had severe acne and one patient in each group had Type 2 diabetes mellitus but neither of these was on oral hypoglycaemic drugs or insulin.

TABLE I
CLINICAL DATA ON THE 97 PATIENTS ASSESSED

	Econazole	Placebo
Number	49	48
Male	21	19
Female	28	29
Age in years	24,1±7,2 (11-47)	26,4±10,1 (11-49)
Duration of rash-weeks	144 ± 68 (50-320)	138 ± 92 (70-260)
Previous treatment:		
selenium sulphide	34	41
other	20	17

At the end of the controlled phase it was found that cures in the econazole group ranged from 53% on day 8 to 69% at day 24 and 32, whilst the corresponding cure rates in the placebo group ranged from 6% to 10%. The differences between the two groups at each assessment visit were significant ($p < 0,001$). The patients' evaluation of their responses to treatment one month after the initial application were also significantly

different at the ($p < 0,001$) level, with 44 of the 47 patients on econazole claiming an improvement and 3 ascribing no change, while only 8 of the 44 patients remaining at the end of 32 days after the application of the placebo foaming solution felt they were improved. These figures coincided exactly with the two investigators' clinical impressions prior to Wood's light and microscopic examination.

SIDE-EFFECTS

There were no side-effects reported or observed in either group. Furthermore, both solutions were found to be aesthetically satisfactory by all patients, despite the need to allow the lather to dry on the body and hair after each application.

CULTURES

Of the 100 patients we were able to obtain cultures of the yeast form of *P. orbicularis* in 84 cases at one or other phase of the study. However, and not surprisingly, it was soon apparent that cultures could not be used as a means of assessing the results of therapy as positive cultures were often obtained when microscopy and Wood's light examination were negative, confirming previous work showing that positive cultures can be obtained from the normal skin of over 90% of adults.²

RESULTS. OPEN PHASE

Twelve patients were excluded from the open phase of the study. These included the nine patients who did not complete the controlled phase of the study and three patients who remained clear after using placebo foaming solution. Three other patients who appeared initially to respond to the placebo solution and subsequently relapsed were also given a course of econazole-base solution some four months after they had received the placebo and were also followed up in the open study. One patient who had originally used econazole solution but did not report for the last (32 day) assessment in the double-blind phase, was considered as a relapse even though he was clear at his last visit at 24 days. This meant that 88 patients could be assessed in the open phase of the study.

All of these patients were seen at monthly intervals and assessed by microscopy and Wood's light until such time as relapses occurred. Any patients who did not attend for follow-up were considered as having relapsed, even though some of them, when seen subsequently for intercurrent illnesses, were still clear. This attitude to the assessment of the results contrasts with that of another worker, who, when evaluating the follow-up results of a trial of the systemic imidazole ketoconazole contented himself with telephonic assessment in two-thirds of the patients followed up.⁷ At the time of reporting (just over three years after the original application of the econazole solution) there are still 22 patients who have continued clear of the disorder, that is, 25% of the original 88 from the open phase.

DISCUSSION

Although tinea versicolor seldom causes symptoms apart from its cosmetic effects, in a climate like that of Durban which allows of year-round bathing it can be a source of great distress for young patients. The disorder

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is unusual in that it can be "cured" by a large number of topical preparations but nearly always recurs. As long ago as 1960 Ruth Burke¹³ pointed out in an address to the Society for Investigative Dermatology that "individuals with this disease must have certain factors which make them susceptible". This should be self-evident if one accepts:

- that *P. orbiculare* is the causative organism and
- that almost all adults have the organism on their skin and
- only a minority develop tinea versicolor.

Many of these susceptibility factors have already been identified such as high temperature and humidity, occlusion, seborrhoeic dermatitis, pregnancy, malnutrition, raised plasma cortisol levels as well as certain immunological factors such as depressed cellular immunity^{14,15}, but these do not account for all cases of frequently relapsing tinea versicolor. Further research on this common tropical fungal infection would need to focus further on those biochemical and immunological changes in the micro-environment of the skin which enable *P. orbiculare* to produce hyphae, to leave its usual rôle of skin commensal and become invasive.

Tinea Versicolor is the commonest superficial fungal disease in tropical & sub-tropical regions.

Until such time as we can prevent this mycelial conversion we shall have to content ourselves with searching for an inexpensive, safe and easy to use preparation which either has long-term efficacy or can be used with safety intermittently and prophylactically. Our study indicates that econazole foaming solution is safe and effective. In choosing to use only three applications the very real risk of poor compliance had to be considered, bearing in mind that we were expecting subjects not only to shampoo every night but also to allow the lather to dry on the hair and body without

rinsing.

With a view to examining the long-term efficacy of the preparation when used intermittently prophylactically we used econazole foaming solution for a total of ten days on the body only, leaving on the lather for 20 minutes and then rinsing and drying. In 15 cases of extensive tinea versicolor this regime resulted in mycological cure and following this initial treatment a single application once a month thereafter has kept all 15 patients free from relapse for 24 months now.

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