THE USE OF NAFTIFINE (EXODERIL) CREAM IN THE TREATMENT OF DERMATOPHYTOSIS

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SYNOPSIS

In an open clinical trial, 108 patients with clinical dermatophytosis with positive smear for mycelium were treated with naftifine 1% cream applied once daily for 4 weeks. Of these, 56 (51.8%) patients had positive culture results at the first visit. However, only 28 (50%) of these 56 patients returned for follow-up visits 1, 2 and 4 weeks after therapy. Mycological cure at the end of 4 weeks was achieved in 26 of these 28 patients, giving rise to a cure rate of 92.9%.

Side effects were found in 10 (9.3%) out of the 108 patients treated. They included irritation, burning and one case of allergic contact dermatitis.

INTRODUCTION

Naftifine (Exoderil, SN 105-843), a naphthyl alkylamine derivative, is a new topical antimycotic. It is fungicidal against dermatophytes and fungistatic against yeasts, molds and other fungi (1, 2). It also has bactericidal properties against both gram positive and gram negative bacteria. It shows an extremely high affinity to the skin. The active substance is slowly released from the horny layer with still approximately 80% unmetabolised, active substance available after 24 hours. Percutaneous absorption of naftifine is minimal. Clinical trials elsewhere have shown the efficacy and the safety of naftifine in the treatment of dermatophyte infections (3, 4, 5).

The present study is an open, systematic, clinical therapeutic study of the antimycotic effect and the safety of naftifine 1% cream in local patients with tinea cruris, tinea corporis or both.

PATIENTS AND METHOD

108 patients with clinical tinea cruris or corporis or both and positive smear for mycelium were recruited into the study. All patients were seen at the Middle Road Hospital Outpatient Clinics from November 1983 to April 1985. Subjects with concomitant onychomycosis or receiving antimycotic agent or antibiotic in the preceding 2 weeks were excluded from the study.

After the first visit, all the patients were followed up 1 week, 2 weeks and 4 weeks after treatment. Pruritus, erythema, scaling, vesiculation, pustulation, thickening, exudation and maceration were assessed every visit, using a six-point rating scale.

0 = absent;
1 = absent to mild;
2 = mild;
3 = mild to moderate;
4 = moderate;
5 = moderate to severe;
6 = severe

The patients were supplied with naftifine 1% cream to apply once daily for 4 weeks to the affected area, and also an one inch wide area of ajacent clinically healthy skin. The side effects on follow-up visits were recorded and graded as mild, moderate and severe. The side effect enquired included burning, itching, dryness and others.

Direct microscopy and culture of the skin scrapings were done for all patients on every visit. The cultures were done on every visit on Mycobiotic agar (Difco laboratories).

RESULTS

Of the 108 patients studied only 56 (51.8%) had positive mycological cultures on the initial visit. Table 1 shows the age, race and sex distribution of these 56 patients. 22 patients suffered from Tinea Cruris, 17 patients from Tinea Corporis and 17 from both Tinea Cruris and Corporis.

Trichophyton mentagrophytes wass identified in 29 (51.8%) patients, and Tinea rubrum in 23 (41%) patients while Epidermophyton floccosum was identified as the causative agent in 4 (7.2%) patients.

37 (66%) patients did not receive any treatment prior to this study, while the remainder had previously been treated with Whitfield's oimtment, Griseofulvin, Chinese medicine, Daktarin or Daktacort. Out of 56 patients who had positive mycological cultures on the first visit, only 28 (50%) patients returned for the scheduled follow-up visits 1, 2 and 4 weeks after treatment. Analysis of the symptoms and signs, mycological scrapings and the culture results was therefore done on these 28 patients only.

Table 2 summarises the results obtained by microscopic examination and culture. At the end of 4 weeks, 26 out of the initial 28 patients had negative culture results, giving rise to a mycological cure rate of 92.9%. The results after 1 to 2 weeks of therapy could not be commented on because cultures were not done on some patients.

TABLE 2: MYCOLOGICAL RESULTS OF 28 PATIENTS WITH COMPLETE FOLLOW-UP

	Before Therapy	After week 1	After week 2	After week 4
Culture —				
positive	28	2	2	2
negative	0	21	14	26
not done	0	5	12	0
Microscopy —				
positive	28	13	4	3
negative	0	15	23	24
not done	0	0	1	1

The cure rate based on direct microscopy results was lower as the direct microscopy of skin scrapings produce more false positive results.

To quantify the clinical response to therapy, the total scores for all the clinical symptoms and those for itch and scaling separately were recorded and the degrees of improvement during the follow-up visits, calculated (Table 3). There was a dramatic clinical response after 1 week of therapy, followed by a steady improvement in the subsequent 4 weeks. In those patients who were symptomatic at the end of 4 weeks, erythema and/or scaling were noted but these were mostly mild in severity.

The side effects in this study were based on all the 108 patients recruited. 4 patients each complained of irritation and burning sensations respectively. These side effects occurred within the first two weeks of therapy. They lasted from one to two days. One patient developed severe itchiness after application of the

TABLE 1: DISTRIBUTION OF PATIENTS BY AGE, RACE, AND SEX

Age	Race			Sex		Total
	Chinese	Malays	Indians	Males	Female	
10—19	12	5	2	18	1	19
20—29	6	5	7	15	3	18
30—39	3	2	2	4	3	7
40—49	2	1	0	1	2	3
50—59	2	1	3			4
60—69	1	1	1	2	1	3
70—79	1	1	0	1	1	2
Total:	27 (48%)	17 (30%)	12 (22%)	42	14	56

TABLE 3: SUM SCORES FOR CLINICAL SYMPTOMS FOR 28 PATIENTS WITH COMPLETE FOLLOW-UP

	Before Therapy	After week (% improvement)		
		1	2	4
All symptoms	380	161 (57.6%)	47 (87.6%)	19 (95%)
Itch alone	111	42 (62%)	16 (85.6%)	6 (94.6%)
Scaling alone	123	61 (50.4%)	14 (88.6%)	9 (92.7%)

naftifine cream and a patch test subsequently showed that the patient had developed an allergic contact dermatitis to the cream. The patient declined further patch testing to the individual constituents of the cream.

DISCUSSION

Dermatophyte infections are common world wide, including Singapore. In Middle Road Hospital, which is the main hospital for diseases of the skin and venereal diseases in Singapore, Dermatophyte infections accounted for 5.2% (1872/35, 920) of all the skin cases seen in the outpatient clinics in the year 1984 (6). Most doctors prescribe Whitfield's ointment as it is the cheapest preparation available. However, it has high failure rates and causes considerable skin irritation. The alternatives prescribed are miconazole and clotrimazole, which are imidazole derivatives. They are effective but expensive and have to be applied twice daily. A less expensive but equally effective and safe topical antimycotic agent is therefore desirable.

The results of this study showed that there is a rapid and substantial symptomatic improvement to naftifine 1% cream in all the patients including the two patients whose culture remained positive at the end of 4 weeks of therapy. Our mycological cure rate of 92.9% at the end of 4 weeks of therapy is remarkable. O'male et al (7) found that naftifine 1% cream is as good as clotrimazole 1% cream and tolnaftaie 1% cream in the treatment of superficial dermatophytosis, the cure rates being 94%, 88% and 98% respectively.

The incidence of the side effects was low and the side effects were mostly minor and evanescent. Similar experience was reported by U Ganzinger et al (5) and O'male (7).

There was one patient who developed allergic contact dermatitis to the cream. Allergy to the cream has hitherto not been reported and is most likely due to the base rather than to the naftifine itself.

It is interesting to note that in our study, 48%, 30% and 22% of the patients were Chinese, Malays and Indians respectively. The racial composition of the patients visiting Middle Road Hospital is 75% Chinese, 15% Malays and 10% Indians. There seems to be a higher incidence of superficial dermatophytosis in Indians and Malays. This may be related to socio-economic factors or different genetic predisposition but the actual reason remains unknown.

In conclusions, naftifine 1% cream is a safe and effective alternative to other currently available topical antifungal agents with the added advantages of once daily application, fungicidal properties and lower cost (as compared to miconazole cream).

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