July–August 1990, Vol. 29, No. 6

Once-Daily Naftifine Cream 1% in the Treatment of Tinea Cruris and Tinea Corporis

Robert E. Jordon, M.D., Ronald P. Rapini, M.D., Ira H. Rex, Jr., M.D., H. Irving Katz, M.D., Janet G. Hickman, M.D., James W. Bard, M.D., Roland S. Medansky, M.D., Deborah A. Lew-Kaya, Pharm.D., John Sefton, Ph.D., Ronald E. DeGryse, M.S., and Frank P. Killey, Ph.D.

From the Department of Medicine, University of Texas Health Science Center, Houston, Texas, Fall River, Massachusetts, Dermatology Clinical Research, Diseases of the Skin Clinic, Minneapolis, Minnesota, Education and Research Foundation, Lynchburg, Virginia, Lexington Clinic, Lexington, Kentucky, Chicago, Illinois, and the Department of Clinical Research and Development, Herbert Laboratories, Irvine, California

ABSTRACT: Seventy patients with tinea cruris or tinea corporis were treated with naftifine cream 1% or vehicle once daily for 4 weeks in this double-blind, randomized study. After two weeks, the patients using naftifine had a significantly higher mycologic cure rate than the vehicle-treated patients (79% vs. 31%, $p < 0.001$), and they showed significantly better resolution of signs and symptoms. Statistically significant differences favoring naftifine over its vehicle were found throughout the treatment period and 2 weeks posttreatment.

Compared with various imidazole drugs, the topical antifungal agent naftifine has been shown to provide both a more rapid mycologic cure and earlier symptomatic improvement in dermatomycoses.[1,2] One factor that may contribute to the efficacy of naftifine is its ability to penetrate the epithelium and accumulate in the upper cutaneous layers to levels much higher than the minimum inhibitory concentrations for dermatophytes.[3] Gradual liberation of the drug from these layers may prolong the fungicidal action of a single application. Longer duration of action may in turn allow application frequency to be reduced from twice daily to once daily without compromising efficacy.

Methods and Materials

The study population included 57 men and 13 women ranging in age from 14 to 67 years with a mean age of 40.6 years. The diagnosis of tinea cruris or tinea corporis was confirmed by potassium hydroxide microscopy and culture. Baseline culture results revealed the presence of the following dermatophytes: *Trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum,* and *Microsporum canis.* Of the dermatophytes identified, 71% were *T. rubrum* and 14% were *T. mentagrophytes.*

Patients were randomly assigned to treatment groups (33 patients to the naftifine group and 37 to the vehicle group) and instructed to apply their cream preparations once daily for 4 weeks. Potassium hydroxide microscopy, fungal culture, and an assessment of signs and symptoms were performed after 2 and 4 weeks and again 2 weeks posttreatment.

The rate of mycologic cure (negative microscopy and culture) was determined for each treatment at each examination and compared between treatments with chi-square analysis or Fisher's exact test. The severity of signs and symptoms was compared between treatments with the Wilcoxon-Mann-Whitney test.

Table 1. *Rate of Mycologic Cure, Defined as Negative Microscopy and Negative Culture*

Week	Naftifine	Vehicle	p Value
2	79% (26/33)	31% (10/32)	<0.001
4	86% (25/29)	30% (10/33)	<0.001
6*	66% (19/29)	26% (8/31)	0.002

* Two weeks posttreatment.

Address correspondence to: Deborah A. Lew-Kaya, Pharm.D., Herbert Laboratories, 2525 Dupont Drive, Irvine, CA 92715.

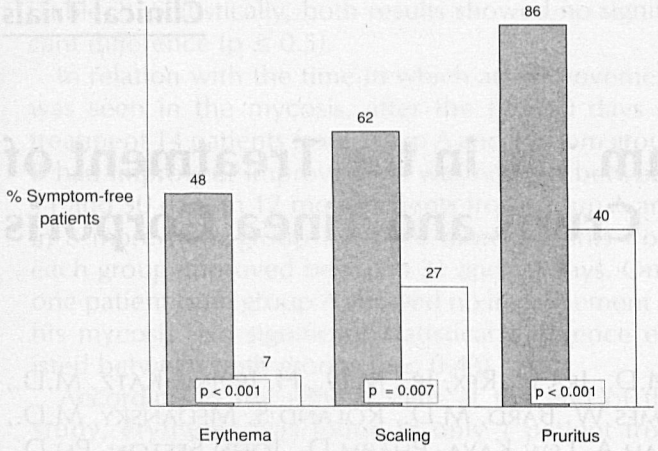

FIG. 1. Resolution of signs and symptoms: percentage of patients who were free of erythema, scaling, and pruritus after 4 weeks of once-daily treatment with naftifine cream or vehicle (p values based on the distribution of severity scores). ■: Naftifine; □: vehicle.

Results

Naftifine cream, applied once daily, was highly active in the treatment of tinea cruris and tinea corporis, as shown by a rapid increase in mycologic cure rate (Table 1). After only 2 weeks of treatment the cure rate was 79% for naftifine-treated patients and 31% for vehicle-treated patients ($p < 0.001$). A significantly higher cure rate for the naftifine group was also noted at the last examination during treatment (week 4) and 2 weeks posttreatment (week 6).

Improvement in signs and symptoms, based on reductions in incidence and severity, was more rapid and more pronounced among the patients using naftifine. After 2 weeks of treatment erythema, papulation, and fissuring were significantly less severe in the naftifine group compared with the vehicle group. By the fourth week the naftifine group also had significantly less severe vesiculation, scaling, crusting, and pruritus. Figure 1 shows the percentages of patients who were free of erythema, scaling, and pruritus at the end of treatment.

Side effects requiring withdrawal from the study were reported for two patients using vehicle (severe edema and erythema for one patient and severe pruritus for the other). No side effects were reported for patients using naftifine.

Discussion

As indicated by both a high mycologic cure rate and improvement in all signs and symptoms, naftifine cream 1% in a once-daily regimen was a highly successful treatment for tinea cruris and tinea corporis. This finding is consistent with previously published European data suggesting a high level of efficacy when once-daily naftifine is used in the treatment of dermatomycoses.[3,4] Administered once daily, naftifine may offer the added practical benefit of improved compliance, an important variable in the management of fungal infections.

Particularly noteworthy in our results is the pattern of early response to treatment in the patients using naftifine. Similar early naftifine action was shown in which a twice-daily regimen of naftifine or econazole was used in the treatment of tinea cruris or tinea corporis.[2] The early resolution of symptoms afforded by naftifine in this study and others may be due to an anti-inflammatory activity. Both animal[5] and human[6,7] studies indicate that naftifine possesses anti-inflammatory properties. An anti-inflammatory effect of naftifine on human skin has been shown by suppression of the erythema response to ultraviolet light.[6] Naftifine and a combination of econazole and triamcinolone acetonide were compared in patients with inflammatory dermatomycoses; naftifine was as effective as the antifungal/corticosteroid combination in reducing the signs of inflammation.[7]

Drug Name

Naftifine cream 1%: Naftin

References

1. Nolting S, Weidinger G. Naftifine in severe dermatomycosis: econazole-controlled therapeutic comparison. Mykosen. 1987;30(suppl 1):70–77.
2. Millikan LE, Galen WK, Gewirtzman GB, et al. Naftifine cream 1% versus econazole cream 1% in the treatment of tinea cruris and tinea corporis. J Am Acad Dermatol. 1988;18:52–56.
3. Meinicke K, Striegel C, Weidinger G. Treatment of dermatomycoses with naftifine: therapeutic efficacy on application once daily and twice daily. Mykosen. 1987;30(suppl 1):98–103.
4. Polemann G. Antifungal efficacy of naftifine applied once daily. Mykosen. 1987;30(suppl 1):92–97.
5. Petranyi G. Preclinical evaluation of Exoderil (naftifine): I. Results of experimental studies of the antifungal activity profile. Mykosen. 1987;30(suppl 1):22–27.
6. Jung EG. The anti-inflammatory efficacy of naftifine as evaluated from the erythema response to ultraviolet light. Mykosen. 1987;30(suppl 1):88–91.
7. Tronnier H. Inflammatory dermatomycoses: comparative study of naftifine and a combination of a corticosteroid and an imidazole derivative. Mykosen. 1987;30(suppl 1):78–87.