mykosen | mykosen 29 (1) 41–44
accepted/angenommen: 10. September 1985

A Double Blind Evaluation of Fenticonazole Cream 2% and Clotrimazole Cream 1% in Dermatomycoses

Doppelblindstudie mit Fenticonazol-Creme 2%ig und Clotrimazol-Creme 1%ig bei Dermatomykosen

A. Finzi*, A. Fioroni*, P. Monici Preti** and M. Mounari**

*Department of Dermatology, University of Milan School of Medicine

**Recordati Medical Department

Key words: dermatomycoses - fenticonazole - clotrimazole
Schlüsselwörter: Dermatomykosen - Fenticonazol - Clotrimazol

Summary: 21 patients suffering from dermatomycoses were randomly assigned either to 2% fenticonazole cream or 1% clotrimazole cream.
The study was performed under double-blind conditions and on patients, with symmetrical or clinically comparable lesions.
Patients were evaluated, clinically, microscopically and by culture before entering the study and then at weekly intervals for four weeks. The cream was applied twice daily.
Eighteen lesions from the 21 treated with fenticonazole 2% cream and 13 lesions out of 21 treated with clotrimazole 1% cream were definitely cured. The differences between the two treatments were statistically significant in favour of fenticonazole in the third week of treatment ($p < 0.05$ - chi square test).

Zusammenfassung: 21 Patienten mit Dermatomykosen, die symmetrisch lokalisiert und klinisch vergleichbar waren, wurden in einer Doppelblindstudie seitenvergleichend mit 2% Fenticonazol-Creme und 1% Clotrimazol-Creme behandelt. Klinische, mikroskopische und kulturelle Untersuchungen wurden vor Beginn der Behandlung und dann in wöchentlichen Intervallen über 4 Wochen durchgeführt. Die Creme wurde zweimal täglich aufgetragen. Bei 18 von 21 mit Fenticonazol 2%-Creme behandelten Fälle und bei 13 von 21 mit Clotrimazol 1%-Creme behandelten wurde vollständige Abheilung erreicht. In der dritten Behandlungswoche erwies sich das günstigere Behandlungsergebnis mit Fenticonazol als statistisch signifikant ($p < 0{,}05$ - chi Quadrattest).

Introduction

Fenticonazole, an imidazole derivative, is a potent broad-spectrum antimycotic with bactericidal activity in vitro as in vivo, against gram-positive bacteria. In preclinical trials it was found to be very active and safe (1-9).

Dermatophytes, yeast causing agents are the most sensitive among fungi and in previous clinical trials it was shown that fenticonazole is more active than other imidazole derivatives in the treatment of dermatomycoses (10-11).

The aim of this study was to compare fenticonazole with clotrimazole in patients with symmetrical or clinically comparable lesions.

Material and Methods

1) Methods

Twenty-nine patients suffering from dermatomycoses with symmetrical or clinically comparable lesions were treated with fenticonazole 2% cream or clotrimazole 1% cream.

Patients treated with antifungal medication during the previous four weeks were not admitted to the trial.

Patients with history of hypersensitivity to topical medications or suffering from liver disease, epilepsy or with chronic diseases (like hypertension, diabetes, renal and heart failure), not under adequate therapeutic control were also excluded.

The two treatments were identical in packaging and very similar as type of cream.

Other treatments interferring with the drugs under study (immunosuppressant, steroidal, oral antifungal, antibiotic) were not allowed during the period of the study.

The creams were applied twice daily.

The first application was done by a nurse in order to show the patients how to use the treatments.

The number of tubes that the patients were given was sufficient for approximately one-week's application and the remaining quantity had to be controlled every week by the investigator in order to determinne the patient's compliance.

The patients were instructed not to apply any cream twenty-four hours before the weekly control.

Treatment was continued until the cultures (or in case of pityriasis versicolor the direct microscopic examination) became negative, or for a maximum of four weeks.

Patients presenting symptoms of dermatomycoses and with positive microscopic examinations started treatment immediately. Confirmation of the diagnosis and isolation and identification of the pathogenic fungi was done by culture (except in cases of pityriasis versicolor where only microscopic examination was applied). Only patients with confirmed diagnoses (direct microscopy, culture) were finally evaluated. The criteria of evaluation were the following:

a) Microscopic examination
   (cutaneous scrapings suspended in a drop of 10% potassium hydroxide)
b) Culture
   (Sabouraud Dextrose Agar - seven days of growth at 24°C)
c) Symptoms
   (desquamation, redness, itching, vescicles, oedema) were considered as minor criteria of evaluation.

They were examined initially to determine the "equivalence" of the skin lesions (one to be treated with clotrimazole the other with fenticonazole); then the modification of symptoms was followed only to determine if the patient was "cured" or not. The patients were classified "cured" only when both the microscopic examination and the culture were negative together with absence or slightness of symptoms. The patients were classified "improved" in case of absence or slightness of symptoms with positive laboratory findings (microscopic or culture).

2) Patients description

Thirteen males and eight females aged between 20 and 79 years (average 59.3 years) were included in the trial (tab. 1).

The duration of the disease, eventual pretreatment and the relative clinical results are shown in tab. 2; patients suffering from a recent disease (1-4 weeks) or relatively recent (2 weeks - 1 year) or chronic disease are represented in equivalent number. Most of them had a previous unsatisfactory treatment.

The localization of the bilateral dermatomycoses are summarized in tab. 3; in particular, 13 were affected by tinea, 7 by candidiasis and 1 by pityriasis versicolor.

The identification of the fungi is reported in tab. 4; a prevalence of Candida albicans, Epidermophyton floccosum and Trichophyton rubrum was found.

Table 1
Age and sex distribution
of patients with dermatomycoses

Sex	No. of Patients	Age					
		20-29	30-39	40-49	50-59	60-69	70-79
Male	13	1	2	2	3	2	3
Female	8	3	2	-	1	2	-

Table 2
Duration of disease and pretreatment
of patients with dermatomycoses

No. of patients	Duration						Pretreatment		Pretreatment Results		
	Weeks		Months		Years						
	1-2	3-4	2-5	6-12	2	3	yes	not	+	=	-
21	6	1	5	3	4	2	13	8	1	10	2

+ improved = unchanged - worsened

Table 3
Localization of dermatomycoses

No. of Patients	Localizations						
	corporis	Tinea pedis	cruris	Intertrigo	Candidiasis interdigital	Perlèche	Pityriasis versicolor
21	2	5	6	3	3	1	1

Table 4
Identification of pathogenic fungi by microscopical and
cultural examination of bilateral lesions

Mycological Results	No. of Cases	%
Candida albicans	7	33.2
Microsporum canis	1	4.8
Epidermophyton floccosum	5	23.8
Trichopyton rubrum	5	23.8
Pityrosporum orbiculare (Mal. furfur)	1	4.8
Trichopyton rubrum + yeasts	1	4.8
Yeasts (other than C. albicans)	1	4.8

Results and Discussion

The results after four weeks of treatment are shown in table 5. Definite cures were obtained in 18 patients with lesions treated with fenticonazole (86%) and in 13 patients of the clotrimazole treated group (62%). This difference is statistically significant after the third week ($p < 0.05$ in the third week and $p = 0.06$ in the fourth week). The mean time in which definite cure was obtained was 2.3 weeks in those treated with fenticonazole and 3.4 weeks in those treated with clotrimazole.

No adverse drug reactions were observed in either treatment.

The present study shows that fenticonazole 2% gives a more rapid healing and a higher cure rate than clotrimazole 1%.

Table 5
Total cures of lesions treated with fenticonazole and of lesions treated with clotrimazole

	Weeks			
	1	2	3	4
Fenticonazole sites (N = 21)				
Total cures	2	4	5	7
Cure rates (cumulative %)	9.6%	28.5%	52.3%	86%
Clotrimazole sites (N = 21)				
Total cures	1	2	-	10
Cure rates (cumulative %)	4.7%	14.3%	14.3%	62%
Statistical difference (Chi squared test)	n.s.	n.s.	$P < 0.05$	$p = 0.06$

We thank Miss Barbara Picchi for her help and advice.

Bibliography

1. Tajana, A., R. Cappelletti, A. Leonardi, D. Nardi & M. Veronese (1981): Synthesis and antimycotic activity of alfa-Aryl-beta, N-imidazolylalkyl Benzyl Ethers, Arzneim. Forsch. (Drug Res.), 31, 2121.
2. Nardi, D., R. Cappalletti, A. Catto, A. Leonardi, A. Tajana & M. Veronese (1981): New alfa-Aryl-beta, N-imidazolylethyl Benzyl and Naphthylmethyl Ethers with antimycotic and antibacterial activity, Ibidem 31, 2123.
3. Tajana, A., C. Sibilla, R. Cappelletti, A. Cova & D. Nardi (1981): Physico-chemical structural and analytical studies on Fenticonazole, a new drug with antimycotic properties, Ibidem 31, 2127.
4. Veronese, M., M. Salvaterra & D. Barzaghi (1981): Fenticonazole, a new imidazole derivative with antibacterial and antifungal activity. In vitro study, Ibidem 31, 2133.
5. Veronese, M., D. Barzaghi & A. Bertoncini (1981): Antifungal activity of Fenticonazole in experimental dermatomycosis and candidiasis, Ibidem 31, 2137.
6. Veronese, M., D. Barzaghi, A. Bertoncini & M. Zadro (1981): The salmonella mutagenicity assay on Fenticonazole, a new antifungal imidazole derivative, Ibidem 31, 2140.
7. Veronese, M., D. Barzaghi, A. Bertoncini & M. Zadro (1981): Mutagenicity studies on Fenticonazole, a new antifungal imidazole derivative, Ibidem 31, 2142.
8. Graziani, G., P. Cazzulani & E. Barbadoro (1981): Toxicological and pharmacological properties of Fenticonazole, a new topical antimycotic, Ibidem 31, 2145.
9. Graziani, G. & P. Cazzulani (1981): Irritation and toxicity studies with Fenticonazole applied topically to the skin and mucous membranes, Ibidem 31, 2152.
10. Stetter, H. (1984): Fenticonazole (2% cream) in the treatment of skin disease due to dermatophytes, Acta Therapeutica, 10, 241-248.
11. Niebauer, G. & E. M. Kokoschka: Treatment of dermatomycoses with topical fenticonazole and econazole - Internal Report in press.

Anschrift: Dr. P. Monici Preti, Medical Dept., Recordati S.P.A., via Civitali 1, 20148 Milano/ Italy.