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Treatment of Dermatomycoses with Topical Fenticonazole and Econazole

Lokalbehandlung von Dermatomykosen mit Fenticonazol und Econazol

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Summary: Fifty-two patients suffering from dermatomycoses were randomly assigned either to a treatment of fenticonazole 2% cream or to econazole 1% cream in an double blind trial.

Patients were evaluated clinically, microscopically and by culture before entering the study and then at weekly intervals for 4 weeks. The creams were applied twice daily.

24 patients out of the 28 included in the fenticonazole group and only 13 from the included in the econazole group were definitively cured or presented marked improvement (difference statistically significant, $p<0,02$).

The onset of fenticonazole action was more rapid then that of econazole. Complete recovery based on the disappearance of direct microscopic evidence and on clinical healing was noted in 15 patients out of the 28 treated with fenticonazole and in 10 patients out of the 24 treated with econazole.

No side effects were observed in either group.

Zusammenfassung: 52 Patienten mit Dermatomykosen wurden in einer Doppelblindstudie mit entweder 2% Fenticonazol-Creme oder 1% Econazol-Creme behandelt. Die Patienten wurden klinisch und mykologisch vor der Studie und in wöchentlichen Abständen über vier Wochen untersucht. Die Creme wurde 2mal täglich angewendet. 24 von 28 mit Fenticonazol behandelten und 13 von 24 mit Econazol behandelten Patienten wurden vollständig geheilt oder zeigten deutliche Besserung (statistische Signifikanz $p<0,02$). Die Wirkung trat bei Fenticonazol früher als bei Econazol ein. Nebenwirkungen wurden in keiner der beiden Gruppen beobachtet.

Introduction

Fenticonazole, an imidazole derivative, is a potent broad-spectrum antimycotic with bacterial activity, in vitro as in vivo (1, 2, 3, 4) against Gram-positive bacteria (5, 6), dermatophytes, yeasts, dimorphic fungi and aspergilli.

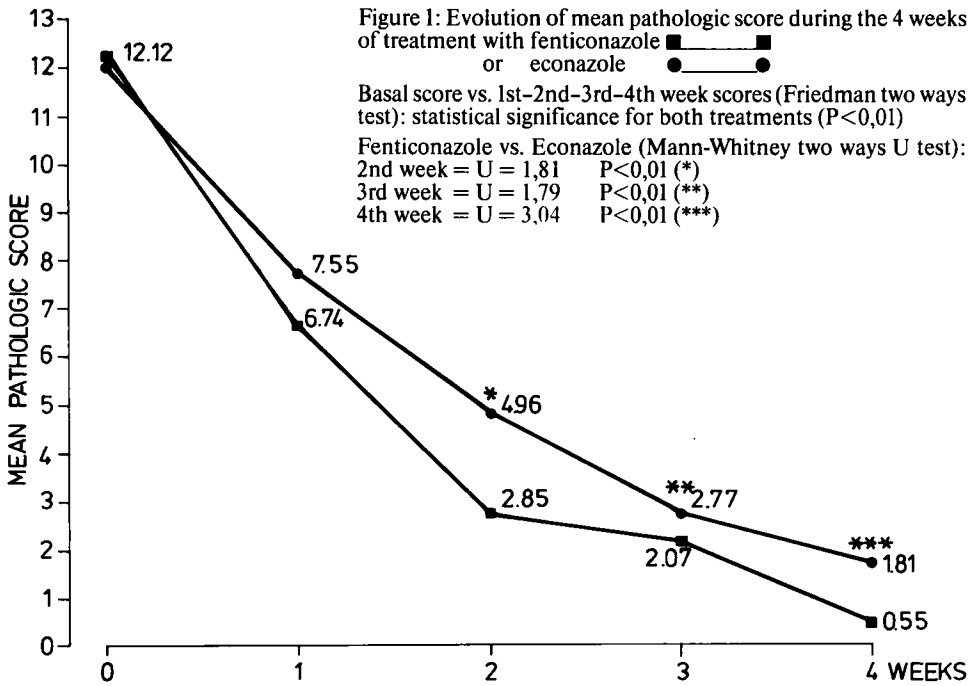

Figure 1: Evolution of mean pathologic score during the 4 weeks of treatment with fenticonazole ■——■ or econazole ●——●

Basal score vs. 1st-2nd-3rd-4th week scores (Friedman two ways test): statistical significance for both treatments ($P<0,01$)

Fenticonazole vs. Econazole (Mann-Whitney two ways U test):
2nd week = U = 1,81 $P<0,01$ (*)
3rd week = U = 1,79 $P<0,01$ (**)
4th week = U = 3,04 $P<0,01$ (***)

Fenticonazole was found to be both fungistatic and fungicidal. The data obtained in preclinical showed that fenticonazole is more active than other imidazole derivatives like miconazole and clotrimazole. The aim of this study was to compare the clinical efficacy, as well as the tolerance, of fenticonazole 2% cream with econazole 1% in a double blind trial.

Material and Methods

Methods

Fifty-two patients suffering from acute recurrent dermatomycoses or pityriasis versicolor were randomly assigned to the treatments.

Patients suffering from severe hypertension, liver disease, severe renal or heart failure or suffering from chronic diseases not therapeutically controlled were excluded from the trial.

Patients treated with antifungal medications during the preceding four weeks or with a history of hypersensitivity reactions to topical medications were also excluded.

Both the treatments (fenticonazole 2%, econazole 1%) were identical in packaging and type of cream, and were applied to the infected areas twice daily.

Other topical or systemic antifungal therapies or treatments interfering with the drug under study (e.g. steroids, immunosuppressant) were not allowed.

Only patients presenting symptoms of dermatomycoses and with positive microscopic examination were admitted to the trial.

Diagnosis by isolation and identification of the pathogen fungi were subsequently done by culture and only patients with confirmed diagnosis were considered "eligible for the trial".

The treatment was continued until the cultures became negative or for a maximum of four weeks.

Both clinical and laboratory (microscopy and culture) examinations were done at weekly intervals.

Table 1
Strains isolated

Strains	Treatments: Fenticonazole N° of patients	Treatments: Econazole N° of patients
Trichophyton rubrum	9	8
Trichophyton mentagrophytes	2	4
Epidermophyton floccosum	1	1
Microsporum canis	1	-
Pityrosporum orbiculare	2	1
Candida Albicans	13	10
Total	28	24

Table 2
Localization of Dermatomycoses

Localizations	Treatments: Fenticonazole N° of patients	Treatments: Econazole N° of patients
Feet	9	10
Hands	3	3
Genito-femoral folds	5	6
Intergluteal region	1	1
Head	2	1
Tibial region	2	2
Trunk	4	0
Submammary region	2	1
Total	28	24

Table 3
Frequency of Subjective Symptoms and Objective Findings in the Baseline Period in Fenticonazole and Econazole Groups

Symptoms	Treatments: Fenticonazole N° of patients	Treatments: Econazole N° of patients
Desquamation	26	23
Redness	28	23
Itching	20	23
Vesicles	14	12
Oedema	13	10

$P > 0,05$ Mann Whitney U test

In order to make a correct laboratory assessement the patients were instructed not to apply any cream for 24 hours before the weekly control. The following symptoms were evaluated: desquamation, redness, itching, vesicles, oedema.
Clinical evaluation of these symptoms was done according to the following scale:
5 = very intense; 3 = intense; 1 = slight; 0 = absent.

Healing of the mycotic lesions was assessed weekly controlling cutaneous scrapings by direct examination (suspended in a drop of 10% potassium hydroxide) and by culture on Sabourraud Dextrose agar (after seven days of growth at 24°C).

For the complete clinical assessment the following criteria were used:

0 = no improvement: positive lab. (both direct microscopic examination and culture) + symptoms unchanged
1 = slight improvement: positive lab. (both direct microscopic examination and culture) + symptoms reduced
2 = marked improvement: positive lab. (direct microscopic examination and/or culture) + symptoms absent or slight
3 = healing: negative lab. + symptoms absent or slight

In the cases with slight or absent of symptoms, the patients had to be treated for a further week while awaiting the results of the culture. Local and general side effects were checked and recorded in the clinical record form. The following laboratory investigations were also carried out: ESR, WBC, RBC, Hb, BUM, SGOT, SGPT, alkaline phophatase, blood glucose, urinalysis. They were performed at baseline and at the end of treatment. In the case of appearance of severe local systemic side effects the treatment would have to be withdrawn.

No parametric statistical analysis was applied to determine the difference between the two groups of treatment (chi square, Friedman test, Wilcoxon test, Mann-Whitney-test).

A WANG 1001 computer was used for the statistical calculations.

Patients diseases

Twenty-eight patients (12 males and 16 females) aged between 5 and 84 years (average 47 years) were included in the fenticonazole group and Twenty-four (15 males and 9 females) aged between 23 and 89 years (average 52 years) in the econazole group.

There was a prevalence of adults in the econazole group but this was not statistically significant (Wilcoxon's test).

The type of mycetes (tab. 1), localizations (tab. 2) and clinical symptoms (tab. 3) were equally represented in both groups: only the duration of the disease was not completely similar between the groups because in the group treated with fenticonazole there were more patients with a longer history of mycotic infection (see tab. 4).

The difference is not statistically significant (chi square test).

Results and Discussion

Complete recovery or marked improvement was obtained in 24 patients (85,7%) in the fenticonazole group, and only in 13 patients (54,16%) in the econazole group, this difference being statistically significant (chi square test $p<0,02$) (tab. 5). Considering the regression of the mean pathologic score during the 4 weeks of treatment, we noted that both treatments showed their efficacy after the second week, with statistical significance ($p<0,01$ Friedmann test).

On the other hand, if we consider the improvement of pathologic symptoms comparing the two treatments (fig. 1), fenticonazole was more effective than econazole (Mann-Whitney test $p<0,01$) since from the second week the relief of symptoms in the fenticonazole group was striking and rapid.

Side effects were found neither with fenticonazole nor with econazole.

Laboratory values and urinalysis after the treatment were similar to those at baseline.

Table 4

	Treatments	
Duration of the disease	Fenticonazole N° of patients	Econazole N° of patients
1-7 weeks	10	12
2-6 months	10	9
> 6 months	8	3
Total	28	24
Pretreatment*	11	9

P > 0,05 Mann Whitney U test

*N° of Patients already treated in the past

Table 5
Judgment of improvement in weekly intervals (4 weeks) frequencies in the four rating scale categories

Treatment	week 1				week 2				week 3				week 4*			
Score	0	1	2	3	0	1	2	3	0	1	2	3	0	1	2	3
Fenticonazole	5	18	5	0	1	14	10	3	1	7	11	9	1	3	9	15
Econazole	2	17	5	0	1	12	11	0	0	12	7	5	0	11	3	10

0 = No improvement
1 = Slight improvement
2 = marked improvement
3 = healing

*Fenticonazole Vs. Econazole

P < 0,02 chi square test at week 4

(Score 2 + 3 Vs. Score 0 + 1)

Under our experimental conditions the activity of econazole seems to be less evident than that shown in other clinical trials (9, 10, 11). This is probably due to the 24 hour wash-out period before each weekly control, a schedule of treatment which was identically applied for fenticonazole.

Fenticonazole seems to be a very promising new agent for the therapy of dermatomycoses as already shown in the experimental data in animals and vitro and in other clinical trials (7, 8).

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