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Fenticonazole: A Clinical Trial

Fenticonazol: Ein klinischer Versuch

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Key words: Fenticonazole – antimycotic activity – dermatophytes – yeasts – topical use
Schlüsselwörter: Fenticonazol – antimykotische Wirkung – Dermatophyten – Hefen – Lokalbehandlung

Summary: The activity of Fenticonazole against dermatophytes and pathogenic yeasts was studied. 46 patients affected by superficial mycoses have been treated by 2% Fenticonazole cream for time periods ranging from 13 to 28 days. Complete cure was obtained in 76.1% of cases; no symptoms of both local and general intolerance have been registered.

Zusammenfassung: Die Wirkung von Fenticonazol gegen Dermatophyten und pathogene Hefen wurde untersucht. 46 Patienten mit oberflächlichen Mykosen wurden mit 2% Fenticonazol Creme über 13 bis 28 Tage behandelt. Bei 76,1% der Patienten wurde komplette Abheilung erreicht. Lokale oder generelle Intoleranzerscheinungen wurden nicht beobachtet.

Imidazole derivatives are well known to display a strong fungicidal activity on many dermatophytes and yeasts (1, 2). We studied the effects of fenticonazole (alpha-2.4-dichlorophenyl-beta, N-imidazolylethyl-4-phenylthiobenzyl ether nitrate) (fig. 1), a newly synthesized imidazole derivative, topically applied on a wide spectrum of dermatoses with mycotic aetiology.

Material and Methods

46 patients, 27 males and 19 females, 13 to 79 years old affected by superficial mycoses due to dermatophytes and yeasts were studied. Diagnoses (table 1) were confirmed by direct microscopic examination of skin scrapings in 20% KOH and by culture.

2% fenticonazole in a vanishing cream was applied b. i. d. until complete clinical cure was obtained but in no case longer than 28 days. At the end of the treatment both microscopic and cultural tests were repeated.

Blood and urine tests were performed in 25 patients before and after treatment to detect any possible systemic effect of the drug.

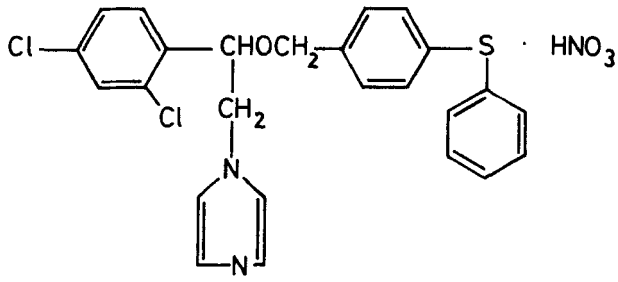

Fig. 1: α-(2,4-dichlorophenyl)-β,N-imidazolylethyl 4-phenylthiobenzyl ether nitrate (fenticonazole, Rec. 15/1476).

Table 1
Diagnoses of patients treated with fenticonazole

Diagnoses	Number of cases	Percentage
Cutaneous mycoses	46	100 %
Pityriasis versicolor	19	41.3%
Tinea corporis	8	17.4%
Tinea cruris	11	23.0%
Tinea pedis	3	6.4%
Candidosis	5	10.9%

The efficacy of the treatment was scored as follows: 0, if after 28 days KOH tests and/or cultures were still positive and the dermatitis still present; 3, if fungi were absent but the dermatitis still present; 6, if treatment succeeded in obtaining both clinical and mycological cure.

The local tolerance was scored as follows: 0, if there were symptoms of intolerance that advised the treatment to be discontinued; 3, if mild symptoms were reported; 6, if tolerance was complete.

In addition, the occurrence of the following reactions was recorded: erythema, erythema and oedema, vesicles and bullae, necrosis. Each of them was scored as absent, slight, modest, severe.

The general tolerance was evaluated during and at the end of the treatment according to the occurrence of systemic allergic reactions and, for 25 patients, to the results of blood (blood cell count, BUN, glucose, alkaline phosphatase, SGOT, SGPT) and urine tests.

Results

Results are shown in table 2. 35 patients (76.1%) proved to be clinically cured; also their laboratory tests (KOH and culture) were negative. 5 patients (10.9%) had partial improvement (mycological tests negative but dermatitis still present) and 6 (13.0%)did not heal at all. Such results have been obtained in time-periods ranging from 13 to 28 days (23.5 as a mean).

Tolerance was always good: no symptoms of local and general intolerance were reported.

The statistical analysis on both blood and urine tests performed in 25 patients did not show any significant difference before and after treatment.

Comment

Fenticonazole is an imidazole derivative, synthesized in the Research Laboratories of Recordati S. p. A. (3), which proved to be both fungistatic and fungicidal against a wide spectrum of

Table 2
Results of topical treatment with fenticonazole

Mycological tests (KOH-culture)	Dermatitis (clinical aspects)	Score	Number of cases	Percentage
negative	cured	6	35	76.1%
negative	not completely cured	3	5	10.9%
positive	not cured	0	6	13.0%

Table 3
Characteristics of patients with mycoses older than one year which had been resistant to other treatments but responded to fenticonazole

Case no.	Duration of the disease (years)	Diagnoses	Localization
2	4	tinea corporis	buttocks
26	3	tinea corporis	coccygeal region
30	3	tinea cruris	groin
31	2	pityriasis versicolor	thorax
35	2	pityriasis versicolor	thorax, back
36	1.5	tinea cruris	groin
44	1	tinea pedis	feet

fungi including dermatophytes and pathogenic yeasts. Its fungicidal activity ranges between 0.312 µg/ml (Trichophyton mentagrophytes and Cryptococcus neoformans) and 160 µg/ml (Aspergillus sp.). Fenticonazole is active also against Candida albicans with highest activity at pH 3.2–5.32 (4). In addition, it shows an excellent activity against Gram positive bacteria with a MIC ranging between 0.009 µg/ml (Staphylococcus aureus) and 5 µg/ml (Clostridium novii) (4).

Scanning electron microscopy has shown that fenticonazole antimycotic activity is due to the gradual and steady destruction of the cytoskeleton, accompanied by a progressive shrinking of the cell membrane. The mechanism of its activity, as for all imidazole derivatives, is not fully clear yet. Recent advances have suggested that fenticonazole may act through the blockade of cytochrome oxidase (with impairment of the cell membrane permeability) and the oxidation-reduction processes (with accumulation of lethal peroxides in the fungal cell (5).

In experimental mycoses fenticonazole displays a strong and fast antimycotic activity against T. mentagrophytes, Microsporum canis and C. albicans (6, 7).

In our study, fenticonazole (2%) in a stable, odourless and well accepted vanishing cream, proved to be effective in 76.1% of cases. Tolerance was always good, as suggested by previous studies on animals in which fenticonazole was tolerated as well as the products used for control (8). Fenticonazole antimycotic activity is to be regarded as excellent, if one considers that 15.2% of our patients had mycoses older than one year that had been resistant to other antimycotics (table 3). It may be that the antibacterial activity of fenticonazole helps its antimycotic activity, since cutaneous mycoses are easily colonized by bacteria which may delay healing.

In conclusion, the efficacy of fenticonazole, its good tolerance and the absence of mutagenic activity (9) suggest this drug as a useful tool in the management of mycotic infections of the skin.

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Buchbesprechung

Grigoriu, Delacretaz, Borelli: **Lehrbuch der medizinischen Mykologie.** 481 Seiten, 655 Abbildungen, 4 Tabellen. Hans Huber Verlag, Bern, 1984. Gebunden DM 230,–.

Das vorliegende Werk wendet sich – nunmehr in einer deutschen Übersetzung – in erster Linie an den mykologisch interessierten Kliniker. Es gliedert sich in sieben Teile mit 55 Kapiteln in bestechend schöner Aufmachung und meist guter bis sehr guter Farbqualität der Abbildungen; dazu kommt ein mykologisches Glossar. Jedes Kapitel wird durch eine Bibliographie verschiedenen Umfangs ergänzt. Einer Tradition entsprechend werden auch einige bakterielle Infektionen (Aktinomykose usw.) behandelt. Rund ein Drittel des Inhalts befaßt sich mit den Dermatophytosen und ihrer Diagnostik, wobei recht gut gelungene Abbildungen die wertvollen Ausführungen über die Materialgewinnung ergänzen. Besonders dieser Teil ist mit einer ungewöhnlichen Vielfalt von klinisch relevanten Ab-