MYCOSES 38, 211–214 (1995) ACCEPTED: DECEMBER 22, 1994

Short therapy for tinea unguium with terbinafine: four different courses of treatment

Terbinafin-Kurztherapie bei Tinea unguium: Vier unterschiedliche Behandlungsvarianten

G. Albanese, R. Di Cintio, C. Martini and A. Nicoletti

Key words. Tinea unguium, antimycotic chemotherapy, short therapy, terbinafine.
Schlüsselwörter. Tinea unguium, antimykotische Chemotherapie, Kurztherapie, Terbinafin.

Summary. Terbinafine has partly solved the well-known problems in the treatment of dermatophyte nail infections. The aim of our study was to assess the effectiveness of very short treatment of dermatophyte nail infections with four different courses of terbinafine with or without chemical onycholysis. For this purpose, 60 patients, divided into four groups, were given different courses of treatment with oral terbinafine. Clinical, mycological and tolerability tests were performed before, during and after treatment. Clear microscopy and culture findings confirmed cure rates in the four groups of 95%, 95%, 70% and 100% without any side-effects. In conclusion, terbinafine has proved to be effective and well tolerated in the very short-term treatment of dermatophyte nail infections.

Zusammenfassung. Terbinafin hat bekannte Probleme in der Behandlung von Dermatophyten-Nagelinfektionen teilweise gelöst. Ziel unserer Studie war, die Validität sehr kurzer Behandlungszeiten mit Terbinafin bei Dermatophyten-Nagelinfektionen in vier unterschiedlichen Behandlungsverläufen mit und ohne Onycholyse zu bewerten. Es wurden 60 Patienten in vier Gruppen eingeteilt, die mit Terbinafin oral nach verschiedenen Schemata behandelt wurden. Klinische Symptomatik, mykologische Befunde sowie Verträglichkeitsbewertungen wurden vor, während und nach der Behandlung erhoben. Eindeutige mikroskopische und kulturelle Ergebnise bestätigten die Heilung in den vier Gruppen zu 95%, 95%, 70% und 100%, ohne daß Nebenwirkungen auftraten. Damit hat sich Terbinafin als effektiv und gut verträglich in der Kurzzeitbehandlung von Dermatophyten-Nagelinfektionen bewährt.

S. Gerardo Hospital, Dermatology Department, Mycology and Tropical Dermatology, Monza (MI), Italy.

Correspondence: Dr G. Albanese, Dermatology Department, Mycology and Tropical Dermatology, S. Gerardo Hospital, Via Donizetti, I-106 20052 Monza (MI), Italy.

Introduction

The treatment of dermatophyte nail infections is particularly problematic since nail laminae are relatively impenetrable to drugs and this topical treatment is practically ineffective. Moreover, oral antimycotics may cause important side-effects since therapy has to last a relatively long time.

The recent introduction of allylamine derivatives, a new class of antifungal agents that can be administered orally, has radically changed the therapeutic outlook for these dermatophyte infections. Terbinafine, in particular, has proved to be not only well tolerated, but also very effective in short-term treatment [1]. We therefore decided to test four different courses of treatment with oral terbinafine with and without chemical onycholysis of the nail lamina.

Patients and methods

All patients admitted to the study were recruited from the Dermatology Department of the San Gerardo Hospital, Monza, Italy. Tables 1–4 show their characteristics, as well as the methods of clinical, mycological and tolerability assessment, treatment and whether or not chemical onycholysis was performed.

Table 1. Group A1 (20 patients)

Sex: M 14, F 6
Mean age: 47 (18–60) years
Mean weight: 73 (45–105) kg
Mean illness duration: 40 (3–120) months
Previous antifungal treatment 6/20
Localization: toenails 19/20
Infecting organism
Trichophyton rubrum 16/20
Trichophyton mentag. 3/20
Microsporum gypseum 1/20

Clinical assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' treatment
4. After 2 months' follow-up
5. After 4 months' follow-up

Mycological assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' treatment
4. After 2 months' follow-up
5. After 4 months' follow-up

Tolerability assessment
Record of adverse drug reactions
Routine haematological and biochemical laboratory tests
Before treatment
After 1 month's treatment
After 2 months' treatment

Therapy
Oral terbinafine 250 mg day^{-1} for 2 months
Atraumatic chemical removal of the nail with 40% aura in Vaseline, followed by occlusive bandage with a rubber thimble for 7 days

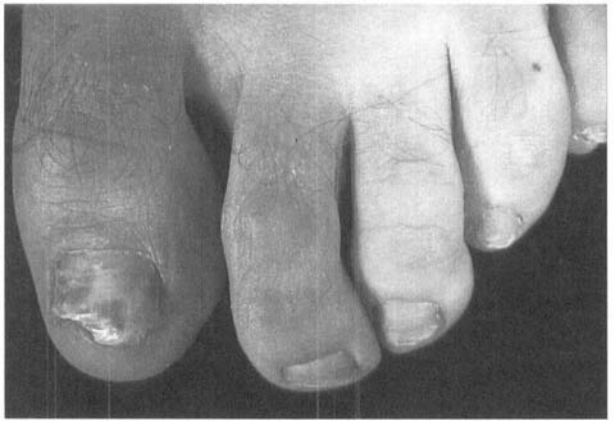

Figure 1. A patient from group B2 before treatment.

Table 2. Group A2 (20 patients)

Sex: M 11, F 9
Mean age: 49 (25–81) years
Mean weight: 72 (58–100) kg
Mean illness duration: 32 (6–120) months
Previous antifungal treatment 3/20
Localization: toenails 20/20
Infecting organism
Trichophyton rubrum 16/20
Trichophyton mentag. 2/20
Epidermophyton floc. 2/20

Clinical assessment
1. Before treatment
2. After 1 month's therapy
3. After 2 months' follow-up
4. After 4 months' follow-up

Mycological assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' follow-up
4. After 4 months' follow-up

Tolerability assessment
Record of adverse drug reactions
Routine haematological and biochemical laboratory tests
Before treatment
After 1 month's treatment

Therapy
Oral terbinafine 250 mg day^{-1} for 1 month
Atraumatic chemical removal of the nail with 40% urea in Vaseline, followed by occlusive bandage with a rubber thimble for 7 days

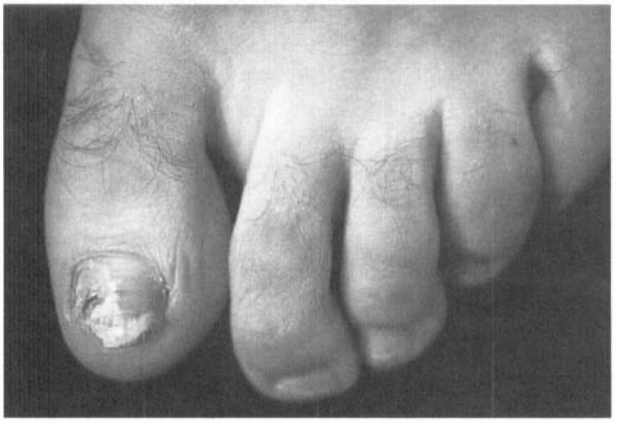

Figure 2. The same patient as in Fig. 1 after 1 month's treatment with terbinafine.

Results

In patients in group A (after chemical oncyholysis) the drug proved to be effective in 95% of cases both in subgroup A1 after 2 months and in subgroup A2 after 1 month. In patients in group B (without chemical onycholysis), efficacy was 70% in subgroup B1 (2 months of daily treatment) and 100% in subgroup B2 (2 months, with weekly administration during the second month).

No side-effects were recorded. The results were verified by microscopy and culture.

Discussion and conclusions

Terbinafine is an antifungal molecule belonging to the class of allylamines and is active when

Table 3. Group B1 (10 patients)

Sex: M 5, F 5
Mean age: 49 (27–73) years
Mean weight: 77 (55–100) kg
Mean illness duration: 118 (3–480) months
Previous antifungal treatment 2/10
Localization: toenails 10/10
Infecting organism
Trichophyton rubrum 10/10

Clinical assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' treatment
4. After 2 months' follow-up
5. After 4 months' follow-up

Mycological assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' treatment
4. After 2 months' follow-up
5. After 4 months' follow-up

Tolerability assessment
Record of adverse drug reactions
Routine haematological and biochemical laboratory tests
Before treatment
After 1 month's treatment
After 2 months' treatment

Therapy
Oral terbinafine 250 mg day^{-1} for 2 months

Table 4. Group B2 (10 patients)

Sex: M 6, F 4
Mean age: 44 (24–69) years
Mean weight: 64 (48–86) kg
Mean illness duration: 39 (1–120) months
Previous antifungal treatment 1/10
Localization: toenails 10/10
Infecting organism
Trichophyton rubrum 10/10

Clinical assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' treatment
4. After 2 months' follow-up
5. After 4 months' follow-up

Mycological assessment
1. Before treatment
2. After 1 month's treatment
3. After 2 months' treatment
4. After 2 months' follow-up
5. After 4 months' follow-up

Tolerability assessment
Record of adverse drug reactions
Routine haematological and biochemical laboratory tests
After 1 month's treatment
After 2 months' treatment

Therapy
Oral terbinafine 250 mg day^{-1} for 1 month and
250 mg once a week for another month

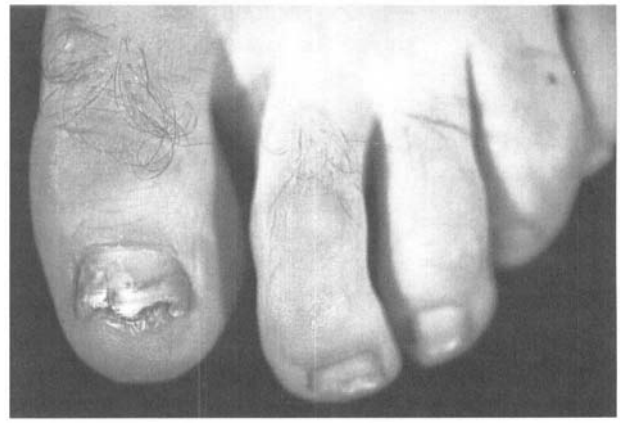

Figure 3. The same patient as in Fig. 1 after 2 month's treatment with terbinafine.

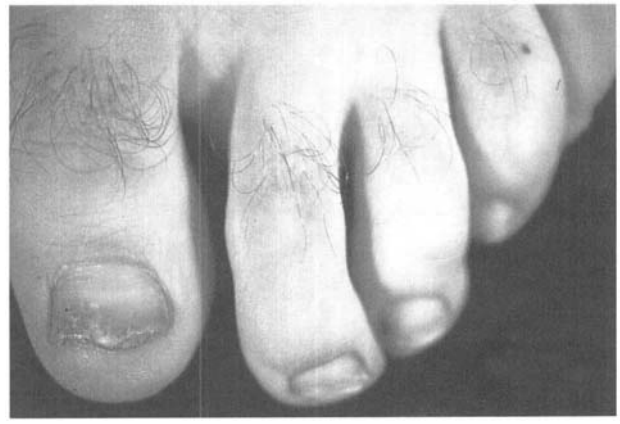

Figure 4. The same patient as in Fig. 1 after 2 month's follow-up.

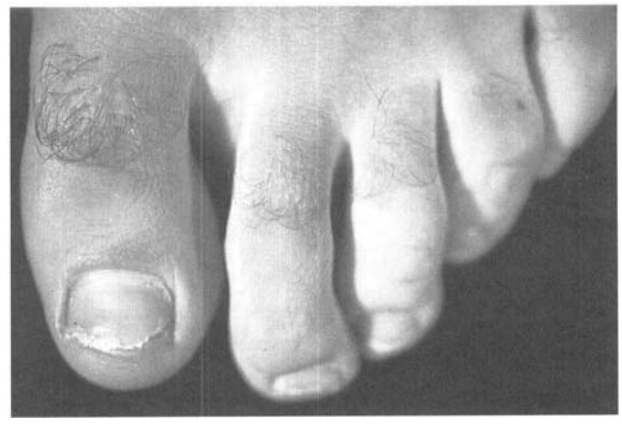

Figure 5. The same patient as in Fig. 1 after 4 month's follow-up.

administered both orally and topically [2]. It has proved to possess fungicidal activity *in vitro* against a wide range of dermatophytes, filamentous and dimorphic fungi, yeasts and Dematiaceae and also some protozan species, in particular *Trypanosoma cruzi* and *Leishmania mexicana mexicana* [3–6].

The mechanism of action of the drug against fungal cells consists in inhibiting the enzyme squalene epoxidase, resulting in a decrease in

membrane ergosterol; the enzymatic blockade results in intercellular accumulation of squalene, which causes irreversible alterations of the fungal cell membrane. Moreover, this fungicidal action does not interfere with the hepatic enzymatic system of cytochrome P450 [7–9]. The efficacy of terbinafine in onychomycosis is mainly due to its relatively rapid diffusion and to its prolonged persistence in the matrix and bed of both affected and healthy nails [10]. Right from the start, the pharmacokinetic and bioavailability data indicated that this drug would be helpful in onychomycoses [11, 12], so the preliminary studies were slightly shorter than those used with previous antimycotics. In our experience, chemical onycholysis did not prove to be essential, although it was useful in cases of marked hyperkeratosis.

The good results of these studies reported in literature and the equally satisfactory results that we obtained with increasingly short periods of treatment confirm the effectiveness of terbinafine in very short-term treatment of tinea unguium.

References

1 Goodfield M. J. D. (1992). Short-duration therapy with terbinafine for dermatophyte onychomycosis: a multicentre trial. *Br. J. Dermatol.* **126**, (Suppl. 39), 33–35.

2 Jensen J. C. (1989) Clinical pharmacokinetics of terbinafine (Lamisil). *Clin. Exp. Dermatol.* **14**, 110–113.

3 Clayton Y. M. (1987) The *in vitro* activity of terbinafine against uncommon fungal pathogens. In: Fromtling, R. A. (ed.) *Recent Trends in the Discovery, Development and Evaluation of Antifungal Agents.* Barcelona: J. R. Prous Science Publishers, pp. 433–439.

4 Goudard, M., Buffard, Y., Ferrari, H. & Regli, P. (1986) *In vitro* activity of a new antifungal agent derived from naftifine, terbinafine (SF 86-327). *Pathol. Biol.*, **34**, 680–683.

5 Goad, L. J., Holz, Jr G. G. & Beach, D. H. (1985) Effect of the allylamine antifungal drug SF 86-327 on the growth and sterol synthesis of *Leishmania mexicana mexicana* promastigotes. *Biochem. Pharmacol.*, **34**, 3785–3788.

6 Meingassner, J. G., Sleytr, U. B. & Petranyi, G. (1983) SF 86-327: effects on the ultrastructure of *Trichophyton mentagrophytes in vitro*. In: Spitzy, K. H., Karrer, K. (eds) (1983) *Proceedings of the 13th International Congress of Chemotherapy.* Vienna, August 28–September 2. Neulengbach: H. Egermann, pp. 25–28.

7 Ryder, N. S. (1983) Specific inhibition of fungal sterol biosynthesis by SF 86-327, a new allylamine antimycotic agent. *Antimicrob. Agents Chemother* **27**, 252–256.

8 Ryder, N. S. (1985) The mechanism of action of terbinafine. *Clin. Exp. Dermatol.* **14**, 98–100.

9 Ryder, N. S. (1989) Inhibition of squalene epoxydase and sterol side-chain methylation by allylamines. *Biochem. Soc. Trans.* **18**, 45–46.

10 Finlay, A. Y., Lever, L., Thomas, R. & Dykes, P. J. (1990) Nail matrix kinetics of oral terbinafine in onychomycosis and normal nails. *J. Dermatol. Tr.* **1**, (Suppl. 2), 51–53.

11 Allen, B. R., Cowley, N., Dawber, R., Evans, E. G. V., Finlay, A. Y., *et al.* (1990). Oral terbinafine: effective in the treatment of chronic nail dermatophytosis. *Br. J. Dermatol.* **121**, (Suppl. 34), 16.

12 Baudraz-Rosselet, F., Rakosi, T., Wili, P. B. & Kenzelmann, R. (1992) Treatment of onychomycosis with terbinafine. *Br. J. Dermatol.* **126**, (Suppl. 39), 40–46.