

Terbinafine (Lamisil) in the Treatment of Mycotic Infection of the Skin and Nails. Experience in Kuwait.

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SUMMARY

Terbinafine (Lamisil, Sandoz) was used in 24 patients suffering from onychomycosis and chronic tinea pedis due to dermatophytes. The dose of the drug was 250mg daily for six weeks in fingernail onychomycosis, for 12 weeks in toenail onychomycosis and for two weeks in chronic tinea pedis. Two patients with fingernail onychomycosis were cured and two improved. In the group of toenail onychomycosis, three patients were cured. Seven patients suffering from chronic tinea pedis were cured and two patients showed improvement clinically, but microscopically remained positive. *Trichophyton rubrum* was the main causative agent in all the three groups.

Introduction

Dermatophytosis is a fungal infection caused by *Trichophyton*, *Epidermophyton* and *Microsporum* group. The disease is a consequence of the host's reaction to the metabolic products of the fungus rather than to the invasion of healthy tissue by the organism.¹ Topical antifungals give good therapeutic results in some forms of dermatophytosis (*tinea cruris*, *corporis* and

interdigitalis). However, these agents are not successful when used for treatment of onychomycosis, *tinea capitis* or chronic *tinea pedis*. In these clinical forms systemic antifungal therapy is fully indicated. Terbinafine (Lamisil) is currently one of the most interesting of a new class of synthetic antimycotic agents; the allylamines.² When taken orally it is fungicidal; inhibiting fungal squalene epoxydase important in the biosynthesis of ergosterol, an essential component of the fungal cell membrane.³

Terbinafine is effective in the treatment of dermatophytic infections of skin and nails,⁴ and its use for these conditions is now licensed in the United Kingdom in both hospital and general practice.⁵ Effectiveness and safety of terbinafine in onychomycosis was confirmed when given for up to 12 months for toenail infections and up to six months for fingernail infections.⁶

We report a study of the effectiveness of terbinafine in patients suffering from chronic infection of feet and onychomycosis due to dermatophytes.

Patients and Methods

Twenty-four patients suffering from

dermatophytic infection of skin and nails entered the trial. Inclusion criteria for patients with onychomycosis and chronic tinea pedis were as follows:

1. Male or female patients above the age of 18 years.
2. Clinical diagnosis of onychomycosis and chronic tinea pedis.
3. Confirmation of diagnosis by positive microscopy and culture for dermatophytes.

Before starting and after stopping the treatment complete blood count, urine routine and liver profile were done. Patients suffering from any systemic disease or condition that might affect the outcome of the study (e.g. liver disease, nephropathy or blood disorders), pregnant or breast-feeding women were all excluded from the study. Patients treated with antifungals one month prior to this study were excluded as well.

Patients with onychomycosis of fingernails were given Terbinafine (Lamisil) 1 tablet daily (250mg) for six weeks. The complete mycological examination (microscopy and culture) was repeated six, 11 and 18 weeks after starting the treatment.

Those patients suffering from onychomycosis of toenails were given the same dose of Terbinafine (Lamisil) i.e. 250mg daily for 12 weeks. Clinical examination was done every four weeks. Microscopy and culture were carried out after stopping the

therapy and repeated after 12 weeks.

Patients with chronic tinea pedis were treated with 250mg of Terbinafine (Lamisil) daily for 14 days. Clinical check-up was done every week during the treatment. The complete mycological examination was repeated six weeks after stopping the therapy.

RESULTS

Fingernail onychomycosis

Five patients entered the trial, four out of this number completed the study without any side effects. The nails cleared in two patients and improved in another two. The worst affected nail plate was that of the thumb (4 cases). The mean duration of infection was 35 months, the mean age of patients was 34 years (Table 1). *Trichophyton rubrum* was isolated from all cases.

Toenail onychomycosis

Seven patients entered the trial, three out of this number completed the study. In one patient the medication was discontinued before the end of the study, because he developed urticarial drug eruption 1 day after starting the therapy. Another patient complained of dizziness and headache two days after starting the therapy. However, the patient successfully completed the trial. In two patients the nails were cleared, in one markedly improved. The worst affected nail

Table 1: Clinical data of the patients

Patients* n=	Diagnosis	Mean duration (months)	Mean age (years)	Cleared	Improved	Failed
4	O.F.N.	35	34	2	2	-
3	O.T.N.	23	38	2	1	-
9	T.P.	58	43	7	2	-

*Number of patients who completed the trial.

O.F.N. = Onychomycosis fingernails.

O.T.N. = Onychomycosis toenails.

T.P. = Tinea pedis.

was that of the big toe (7 cases). The mean duration of infection was 23 months, the mean age of patients was 38 years (Table 1). The distribution of the isolated dermatophytes was as follows: *Trichophyton rubrum* 7 cases, *Trichophyton interdigitale* 3 cases, *Epidermophyton floccosum* 1 case. Negative culture was obtained in one patient with positive microscopy.

Chronic tinea pedis

Twelve patients entered the trial and nine out of this number completed it. In one patient the medication was discontinued because of sweating, bradycardia and palpitations lasting for one day. The treatment was stopped for 3 days. However, after restarting the therapy, the symptoms appeared again. Seven patients were cured, two patients improved clinically but microscopic examination remained positive. The mean duration of infection was 58 months, the mean age of the patients was 43 years (Table 1). The distribution of the isolated dermatophytes was as follows: *Trichophyton rubrum* 7 cases, *Trichophyton interdigitale* 3 cases, *Epidermophyton floccosum* 1 case.

Negative culture was obtained in 1 patient with positive microscopy.

Mild gastrointestinal upset was the major side effect encountered.

Discussion

Systemic anti-fungal treatment is possible with many modalities. Griseofulvin may cause enzyme induction in the liver, which requires a higher dose intake to achieve results. Present therapy with griseofulvin is long, often several months in tinea pedis and up to 18 months for onychomycosis. This is aggravated by high recurrence rates.

Since 1967, many synthetic triazoles and imidazoles have been tested against fungi. Out of this effort, ketoconazole and itraconazole have evolved. Ketoconazole is a very effective drug which must be carefully monitored. Its problems is with liver function, anti-androgenic dysfunction in males, and adrenal dysfunction. There is 1:15,000

incidence of hepatitis that makes dermatologists uncomfortable. Itraconazole, however, so far appears to be quite effective and shows no liver toxicity.⁴

Terbinafine (Lamisil, Sandoz) belongs to the new class of synthetic antifungals, the allylamines. Interaction of Terbinafine with cytochrome P-450 is confined to enzymes active in drug metabolism. Terbinafine does not have the broad inhibition of cytochrome P - 450 that catalyses steps in the synthesis of steroid hormones and prostaglandins.⁷ Terbinafine is therefore not expected to suppress the adrenal axis or effect the gonadal hormones. In addition, Terbinafine is highly lipophilic and is distributed preferentially to the skin as well as fatty tissues. It is released slowly from these tissues. The distribution pattern of Terbinafine may be partially responsible for its high efficacy in chronic diseases of thickened skin or nails.⁸

Terbinafine has several important advantages. First, the treatment takes substantially shorter time (fingernail onychomycosis six weeks, toenail onychomycosis 12 weeks, and chronic tinea pedis two weeks). Griseofulvin which is considered as a standard treatment for onychomycosis must be used for a very long period of time. Furthermore, therapeutic effectiveness of griseofulvin is poor, and cure is achieved in less than 40% of toenail and 70% of fingernail infection. Long course of treatment is one of the major reasons why some patients fail to comply. Second, the side-effect profile of Terbinafine in other studies over 1000 patients (3% gastrointestinal, 1% allergic, 1% others)⁹ has been consistent with the results in this study. No significant side effects were reported in this trial.

Considering that Terbinafine is fungicidal, it has been suggested that it will prove to be an ideal drug as a systemic agent for chronic tinea pedis and onychomycosis.⁴ In our opinion, the drug is indicated in the treatment of chronic dermatophytic infections (onychomycosis and chronic tinea pedis) which are usually recalcitrant to the topical treatment.

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