Terbinafine in the Treatment of Onychomycosis

ONİKOMİKOZ TEDAVİSİNDE TERBİNAFİN

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Summary

Efficiency ofsysreniically used terhinafine in toenail onychomycosis was investigated in this study. Ten cases, diagnosed as onychomycosis clinically and mycologically were treated with terhinafine 250 mg given orally once a day for 12 weeks. At the visit of/burly eight week, 7 of these It) patients were assessed as cured both clinically and mycologically, 2 showed no improvement and 1 had recurrence. Terhinafine was well tolerated in all cases and suggested that it could be a useful agent in the treatment of onychomycoses.

Key Words: Terbinafine, Onychomycosis

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Özet

Bu çalışmada, ayak tırnağı onikomikozlarında sisteınik Terhinafinin etkinliği araştırılmıştır. Klinik ve mikolofik olarak onikomikoz tanısı konulan 10 hasta 12 hafta süre ile günde bir kere 250 mg oral Tcrbinafın ile tedavi edilmiştir. Kültür sonucunda Dermatojit üreyen, tedaviyi tamamlamış ve 4H. hafta kontrolüne gelen 10 hastanın 7'sinde klinik ve mikolojik olarak şifa, 2'siule başarısız sonuç, Kinde relaps elde edilmiştir. İlaç bütün olgularda iyi tolere edilmiş ve onikomikoz tedavisinde önerilebilecek olumlu bir gelişme olarak yorumlanmıştır.

Anahtar Kelimeler: Tcrbinafın, Onikomikoz

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The mam causal agents in onychomycoses which consists of approximately 20% of all nail diseases, arc dermatophytes and Candida. Dermatophytes attack the nail from its free edge and settle down in matrix and hyponychium. Ventral site of the nail plate which is made of soft keratin is infected via hyponychium because of close contact. The nail changes in colour, thickens and crumbles away with minor trauma (1,2).

Onychomycosis is seen in a relatively high rate of 2-5% in population and is the most resistant type of superficial mycoses. Beside no spontaneous remission or cure, recurrences are frequently observed (1,3). Griseofulvine and ketoconazole need long term treatment and both have significant side effects. With new antifungal agents itraconazole and terbinafinc, treatment course is shorter because they diffuse into the matrix and the nail bed and then rapidly into the nail plate. Other antifungals reach only to the matrix and need to be used until the nails regrow (1,4-6). Terbinafinc, a drug of allilamine, has been reported as a very effective agent in oral treatment of dermatophytic onychomycosis (4,7). It inhibits the synthesis of ergosterole which is an important component of fungal cellular membrane. Converting of squalenc to squalcne epoxide by the enzyme squalenc cpoxidasc is blocked with tcrbinafme. Deposition of squalenc results in cellular death (4,5,8). In a few hours following oral intake, terbinafinc can be detected in sebum and stratum corncum. After 24 hours, it can be shown in deeper layers of corncum while detected in distal part of the nail after a 4 weeks (3-18 weeks) of treatment period (6). The early detection in the nail indicates that the diffusion is the major factor for penetration of the drug (4-6).

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Tcrbinafinc is metabolized in the liver and inactive metabolites arc excreted by urine. The recommended dose in the treatment of onychomycosis is 250 mg per day. Daily dose is halved in hepatic disorders and renal diseases those having creatinine elearcnee below 50 mg/ml (4,5). It is recommended to be used in doses of 62,5 mg/day for 40 kg and over. Plasma concentration of terbinafine is increased with use of cimctidine while decreased with rifampicine.lt has no other known drug interaction (4).

Materials and Methods

Our study group have consisted 10 patients who were seen between the dates of December 1994 and February 1995 and who conformed to the following criteria:

A11 cases were healthy adults in general, suffering from toenail onychomycosis, confirmed by microscopic examination and positive culture results for fungi. The species in cases where direct examination with KOH wet mount revealed dermatophytes, were identified by macroscopic and microscopic evaluation of colonics cultured in Sabouraud media with chloramphenicol and actidione.They had not any treatment with oral antifungals in previous 3 months; any gastrointestinal, renal and hepatic disorder or diabetes; pregnancy and use of oral contraceptive drugs; any abnormality in laboratory tests of complete blood count and routine biochemistry

No patient were excluded from the study because of medical reasons such as allergy , intolerance and adverse effects.

Terbinafine in a dose of 250 mg /day orally was given for 12 weeks.

Clinical and mycological examinations were made sequentially in sixth, twelvcth, twentieth and fourty eighth week of therapy. Appearcntly healthy-part of the nails, were measured in length, and ungual changes such as onycholysis, hyperkeratosis, paronychia, deformity and discoloration were noted and scored as 0: absent, 1: mild, 2: marked. Except sixth week, mycological and cultural studies were made at each visit. At the visit of fourty eighth week, cases that showed complete clinical and mycological improvement have been evaluated as "cured", otherwise as "unsuccessful". Cases evaluated as unsuccessful at the end of the study but noted as cured before the final visit, have been accepted as " relapsed". Laboratory tests including complete blood count and biochemical assays of liver enzymes, urea, creatinine and glucose levels have been studied before and at the end of the therapy. Side effects such as gastrointestinal complaints, headache and skin eruptions were recorded at twelvcth week and in the following period.

Results

Of ten patients, 3 were females and 7 males, ages between 26-58 (mean, 47 years). Duration of

Table 1. Clinical and other features of cases with toenail onychomycosis

No:	Duration of infec-tion	0. week *Clin ie	Cultivation	6. week- Clinic	1 -* week Clinic	Culti-vation	20. week Clinic	Culti-vation	48. Week Clinic	Culti-valion	Results	.Adverse effect
1	3 year	0	T.viokiccum	3	s	+	10		18		Cured	-
2	5 year	5	T.totismaus	8	X	+	4	4	+	4	Relapsed	-
3	3 month	5	T. tonsurans	5	5	+	5	+	5	+	Unsuccessful	Dispepsia, nausea
4	10 year	1	T.tonsurans	3	(l	+	8	+	12		Cured	-
5	5 year	0	T.tonsurans	3	s	+	1 s		15		Cured	Nausea
6	7 year	3	1£.floccosum	5	X	+	9		8		Unsuccessful	-
7	20 year	0	H.floccosum	5	7	+	7	+	15		Cured	-
8	2 year	0	E. floccosum	5	10	+	12	+	12		Cured	-
9	3 month	0	T.tonsurans	3	5	+	7	-	12		Cured	-
10	3 year	7	T.rubrum	3	s	+	X	-	13		Cured	-

**The length of uninvolved nail part in nun*
-Represents colonization in Sahoitraud media

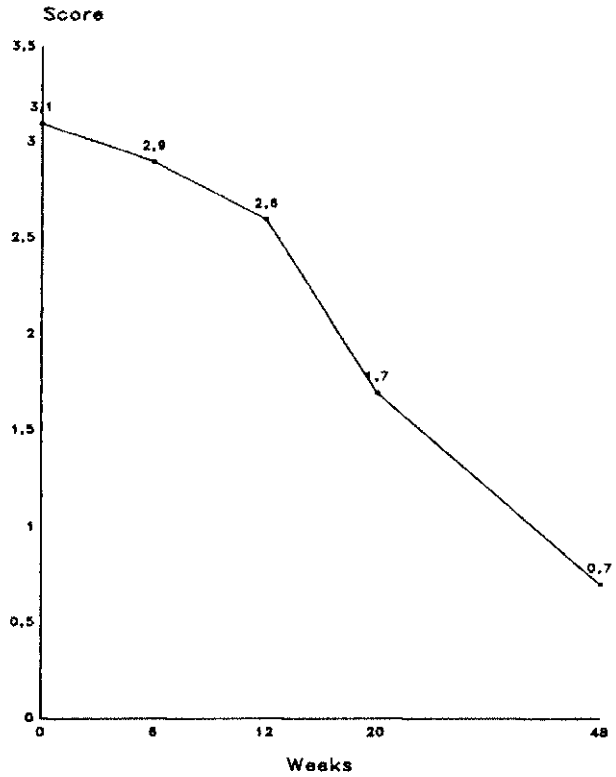

Figure 1. Clinical score in patients with toenail onychomycosis.

the disease was between 3 months and 20 years, with average of 5.8 years.

Table 1 shows clinical and mycological findings, therapy results and adverse effects.Isolated agents were Trichophyton tonsurans in 5 cases, Epidermophyton floecosum in 3, and Trichophyton violaceum and Trichophyton rubrum each in one case. At twelvcth week, all cases had positive microscopic examination and their cultures were also obtained. At twentieth week 6 cases had positive fungi in native preparation and in five of them, dermatophytes determined before treatment, were cultured. At the fourty eighth week, 7 of 10 cases were cured. Two cases were already clear in twentieth week (number 5 and 8). In one of two unsuccessful cases, native examination was positive while cultivation was negative (number 6). The patient numbered 2, showed relaps in twentieth week.

Mean total scores of clinical signs decreased gradually, mostly denoted in twentieth week (Figure 1). Scores were 3.1 before treatment, 1.7 in twentieth week and 0.7 at the end of therapy. Gastrointestinal complaints as nausea and dispepsia were not so severe to stop therapy. Laboratory examinations also showed no abnormality.

Discussion

This study has been programmed to investigate the clinical efficacy and side effects of tcrbinafine (Lamisil) in treatment of dcrmatophytic onychomycosis of toenail. Cure has been obtained m a rate of 70% by 12 weeks treatment. This rate is that of clinical and microbiological elearence at fourty eighth week. Goodfield ct al.(TO) has found this as 82% , Alpsoy et al.(ll) as 79.1%. In another study it has been reported as 85% (12). Our results also have been parallel to those ones above. Rossclctt et al. (13) through a multiccntcr study of 6 months treatment, found the cure rate as 77% for toenail onychomycosis. Schroef ct al. (14) reported the results of cure rates at fourty eighth week as 40% for 6 weeks therapy, 71 % for 12 weeks and 79% for 24 weeks. Our results is the same as Schroef's.

Systemic antifungal agents have been used for a long time in onychomycosis. The main problems in therapy are duration, side effects and patients' compliance. With ketoconazole and griseofulvinc, toenail onychomycosis is treated for 12 months. Success rate with griseofulvine is reported as 30-40% (70% for fingernails) and 50% when toenails were avulsed (11-14).Ketoconazole is more effective than griseofulvine. Both have hepatic side effects. Efficacy of topical antifungals, when used alone, have not yet been determined clearly yet (10).

Our cure rate of 70% belongs to 12 weeks treatment with tcrbinafine. We have observed no adverse effects excluding mild gastrointestinal complaints in two patients. Similar reports have declared the same side effects (11-15). There have been no abnormalities in laboratory tests including complete blood count and hepatic and renal functions.

Results of this study have confirmed that terbinafine is an important milestone in treatment of dermatophyte onychomycosis. Early responses and short courses of therapy increased the patients' compliance. High rates of success and tolerable side effects of terbinafine may make it the drug of choice.

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