

## Miconazole alcoholic solution in the treatment of mycotic nail infections

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### Summary

Nineteen men, suffering from chronic onychomycosis of their toe nails, were treated for 32 weeks with a 2 % miconazole alcoholic solution. Of 20 nails positive by culture before treatment, all were cured clinically and 15 showed no growth of pathogenic fungi six months after treatment. The medication was excellently tolerated.

### Zusammenfassung

Neunzehn männliche Patienten, die mit chronischer Onychomykose der Zehennägel befallen waren, wurden während 32 Wochen mit einer 2 % Miconazole enthaltenden Alkohollösung behandelt. Von den 20 mykologisch positiv gesicherten Nägeln haben sich alle nach Behandlung als klinisch geheilt erwiesen, und bei 15 von ihnen wurden 6 Monate nach Behandlung keine pathogenen Pilze nachgewiesen. Die Miconazol-Lösung wurde ausgezeichnet vertragen.

In recent years, several new drugs have been introduced for the treatment of onychomycosis, by either local or systemic routes. Results have often been disappointing.

In 1971, however, BOTTER (1) reported extremely good results in the treatment of onychomycosis with miconazole 2 % cream. The drug was applied under occlusive bandages and, in some instances, combined with griseofulvin therapy. HEINKE confirmed these findings (2).

Miconazole is a synthetic compound, produced in the laboratories of Janssen Pharmaceutica. It has proved to be active against most fungi, including dermatophytes and yeasts, and against gram-positive bacteria, both *in vitro* (3) and *in vivo* (1, 4, 5, 6).

When the drug became available as a film forming alcoholic solution,\* the advantages of this formulation over the cream for the treatment of onychomycosis were obvious, i. e. easy application of the drug and inconspicuousness of the treatment.

In the present paper we report on the first clinical evaluation of 2 % miconazole alcoholic solution.

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* Formula: miconazole base	0.2	gram
carbosept No. 525	0.475	gram
carbosept No. 515	0.025	gram
propylene glycol U. S. P.	2	gram
ethanol U. S. P. ad	10	ml

**Key words:** Miconazole alcoholic solution, onychomycosis, dermatophytes, yeasts.

Table 1: Individual case data; causative fungi and severity of lesions before treatment

Patient No.	Age	Fungal etiology			
		Left food Fungus	Severity of lesion	Right food Fungus	Severity of lesion
1	67	Trichophyton mentagrophytes	+++	negative	+++
2	68	T. mentagrophytes	+++	—**	0
3	78	T. rubrum	+++	negative	+++
4	36	T. mentagrophytes	+++	Trichosporon cutaneum	+++
5	69	T. mentagrophytes	++	T. mentagrophytes	++
6	42	negative	+++	T. mentagrophytes	+++
7	69	T. mentagrophytes	++	T. mentagrophytes	++
8	65	T. rubrum	+++	T. rubrum	++
9	65	negative	+++	T. rubrum	+++
10	53	positive	+++	T. mentagrophytes	++
11	67	positive	++	T. mentagrophytes	+
12	43	T. mentagrophytes	+++	T. mentagrophytes	+++
13	44	negative	+++	negative	+++
14	37	Candida tropicalis	++	negative	++
15	49	negative	+++	negative	++
16	37	—*	++	—*	++
17	43	Scopulariopsis brevicaulis	++	S. brevicaulis	++
18	47	negative	++	—**	0
19	30	negative	++	—**	0

0: not affected  
 +: light  
 ++: moderate  
 +++: severe

\*: no mycological examination  
 \*\*: normal nail

### Material and methods

**Patient selection:** Nineteen male long-term in-patients, were selected for the trial (median age: 49 years; range: 30—78 years) (Table 1). All of them presented with clinical signs of onychomycosis of at least the big-toe nails. These included subungual keratosis, discoloration, onycholysis, brittleness of the nails and, in some, paronychia inflammation. The duration of the infections ranged from 2 to 20 years. None of the patients had received antifungal treatment during the last two years.

**Assessments and identification of the etiologic fungi:** Several patients had more than one infected nail. The nails were clinically scored with regard to the severity of the lesions (Table 2). Samples of the affected nails were taken and examined microscopically after potassium hydroxide clearing. Cultures were grown on Sabouraud P. S. and Sabouraud P. S. A. media. Identification of fungi was possible for 20 nails from 14 of the patients. Twelve infections were by *Trichophyton mentagrophytes*, 4 by *T. rubrum*, 2 by *Scopulariopsis brevicaulis*, 1 by *Candida tropicalis* and 1 by *Trichosporon cutaneum*. Two nails positive on microscopical examination, did not yield pathogenic fungi when cultured. Thirteen other nails presented a clinical picture of onychomycosis, but microscopic and cultural investigations were negative. One patient was not present at the time when samples for mycological procedures were taken.

Table 2: Clinical evaluation of healing process during treatment period

Pat. No.	Nail	4 w	8 w	12 w	16 w	20 w	28 w	32 w
1	L	0	0	0	/	//	//	///
	R	0	0	0	/	//	//	///
2	L	0	/	/	//	//	//	///
	R	*	*	*	*	*	*	*
3	L	/	0	//	///	///	**	**
	R	0	0	//	///	///	**	**
4	L	0	/	//	///	///	///	///
	R	0	/	//	///	///	///	///
5	L	/	/	//	///	///	///	///
	R	/	/	//	///	///	///	///
6	L	0	/	/	//	//	//	//
	R	0	/	/	//	//	//	//
7	L	0	0	//	///	///	///	///
	R	0	/	//	///	///	///	///
8	L	0	**	0	0	/	//	///
	R	0	**	/	//	//	//	///
9	L	0	/	/	//	//	//	///
	R	0	0	/	//	//	//	///
10	L	0	0	//	///	///	///	///
	R	0	/	//	///	///	///	///
11	L	0	/	//	///	///	///	///
	R	0	/	//	///	///	///	///
12	L	0	/	//	//	//	///	///
	R	0	/	//	//	//	///	///
13	L	0	0	0	0	/	//	//
	R	0	0	0	/	/	//	//
14	L	**	/	//	//	///	///	///
	R	**	/	//	//	///	///	///
15	L	0	0	0	0	//	//	**
	R	0	/	//	//	///	///	**
16	L	0	0	0	0	/	//	//
	R	0	0	0	0	/	//	//
17	L	0	/	//	///	///	///	///
	R	0	/	//	///	///	///	///
18	L	**	0	/	/	//	//	///
	R	**	*	*	*	*	*	*
19	L	**	0	//	//	//	///	///
	R	**	*	*	*	*	*	*

\*: not affected  
 \*\*: absent  
 Scoring of newly grown, clinically healthy nail  
 0: no growth  
 /: growth up to 50%  
 //: growth up to 75%  
 ///: practically complete or complete cure

*Treatment:* Twice daily, 2% miconazole alcoholic solution was applied to the affected toe nails using the drip-nozzle fitted to the bottles. The solution was allowed sufficient time to dry. Each time the previously applied miconazole film was removed. Special attention was paid to the application under the front edge of the nails along the lateral edges and the cuticles. The treatment lasted 32 weeks, during which time no other anti-fungal therapy was prescribed. Each patient was treated with his own bottle of miconazole.

The nursing staff of the hospital took special care of the hygienic measures taken during the trial. Feet were washed and socks were changed daily. Except for keeping the nails short, no special surgical treatment was applied.

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Table 3: Individual results of mycological examination, 6 months after cessation of treatment

Patient No.	Fungal isolations	
	Left	Right
1	negative	negative
2	negative	negative
3*	—	—
4	negative	negative
5	negative	negative
6	negative	negative
7	<i>T. mentagrophytes</i>	<i>T. mentagrophytes</i>
8	<i>T. mentagrophytes</i>	negative
9	negative	negative
10	negative	negative
11	negative	<i>T. mentagrophytes</i>
12	negative	negative
14	negative	negative
16**	negative	<i>T. rubrum</i>
17***	—	—

\* Patient died before the control examination.

\*\* Not present at first examination.

\*\*\* Not present at control examination.

Patients 13, 15, 18 and 19 were negative before and after treatment.

The aspect of the treated nails was evaluated monthly and the healing process was scored clinically. Six months after cessation of treatment a second mycological examination (microscopic examination and culture) was performed to assess whether a permanent mycological cure had been obtained.

## Results

Table 2 presents the individual clinical evaluation of the healing process and Figure 1 the cumulative evaluation of all treated nails.

After 16 weeks of treatment, more than 80 % of the treated nails showed a positive response to treatment. At the end of the 32-week treatment period, 80 % of the treated nails were virtually cured and in these cases a new and clinically healthy nail had developed.

During the entire treatment period the miconazole alcoholic solution was well tolerated. No adverse local reactions occurred.

Table 3 shows the results of the mycological examination six months after cessation of the treatment in 13 patients. Only 4 of the 17 nails that had been mycologically positive before treatment yielded a pathogenic fungus. In three nails *T. mentagrophytes* was still present. In one nail this fungus was also isolated; although before treatment *T. rubrum* had been recovered. Control samples could not be obtained from two patients (No. 3; No. 17). One patient had not been examined before treatment (No. 16). However after treatment *T. rubrum* was isolated from one nail while in another the microscopic examination was positive but no fungus could be cultured. Clinically, these 4 infected nails showed a picture of developing onychomycosis.

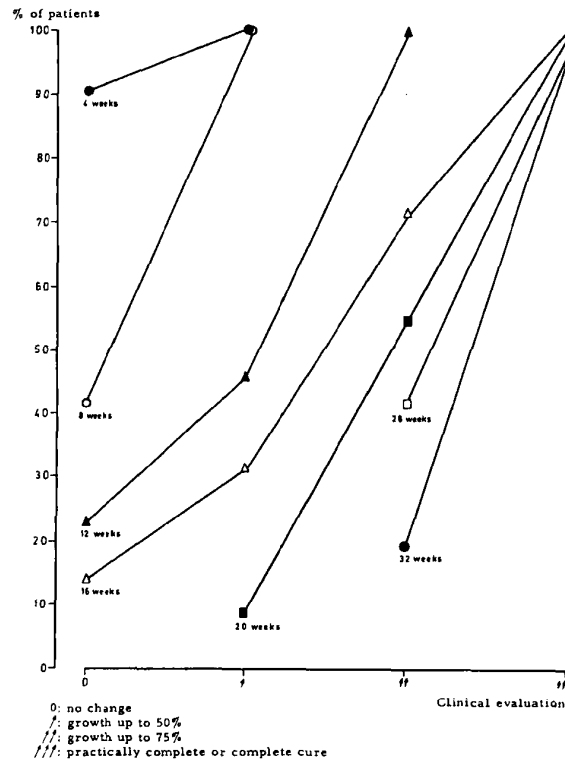


Fig. 1: Cumulative evaluation of nail treatment: all treated nails

### Comments

Clinical experience with miconazole in the treatment of onychomycosis is still limited. Our present study with a 2% miconazole alcoholic solution appears to substantiate the results obtained with 2% miconazole cream by BOTTER and HEINKE (1, 2).

The main advantages of the miconazole solution are its broad spectrum of efficacy against fungi, including yeasts; ease of applicability and the absence of local irritation or allergic manifestations.

It seems that, in long-standing and rooted onychomycoses, such as the cases treated here, miconazole solution is a convenient alternative to treatment with griseofulvin. The duration of treatment appears to be equal but, clearly, a topical application is to be preferred for the treatment of a localized disease such as onychomycosis.

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