

ITRACONAZOLE PULSE THERAPY IN ONYCHOMYCOSIS

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A prospective study of 30 clinically and mycologically diagnosed cases of onychomycosis was carried out for a period of twelve months from May 1996 to April 1997. Itraconazole pulse therapy was given for the 1st week followed by 3 week drug-free period, for 1st 3 months for the finger nail cases and 4 months for finger nail + toe nail and toe nail cases. Patients were evaluated at baseline, week 4, week 12, week 16, week 24, up to 12 months and assessed as cleared or markedly improved with clinical and mycological success. The result of our study is very much encouraging. It suggests that the use of itraconazole pulse therapy will maintain the continuous treatment efficacy and is cost effective than continuous therapy.

Keywords: Onychomycosis, Itraconazole, Pulse therapy

Introduction

Onychomycosis may be caused by dermatophytes, nondermatophyte moulds or yeast. In the treatment of onychomycosis, oral therapies have generally been given as a continuous dosing regimen. Based on the advances of understanding of pharmacokinetics of itraconazole, intermittent pulse dosing therapy was investigated. Itraconazole achieves high levels of concentration in the nail within 7 to 14 days of commencing therapy. It persists in nails for development of short duration of treatment schedule. Numerous European studies have demonstrated the efficacy and safety of three cycles of itraconazole pulse therapy in treatment of toe nail onychomycosis.¹⁻² Itraconazole pulse therapy is equally effective as continuous therapy. Based on these

facts we conducted a study of itraconazole pulse therapy in 30 cases of onychomycosis.

Materials and Methods

(A) Selection of the patients

(1) Thirty clinically and mycologically 'KOH' positive patients were included in the study group (Table 1). Patients undergoing therapy with rifampicin, phenobarbital, phenytoin, carbamazepine, astemizole, terfenadine, and digoxin and those having concurrent therapy with H₂-antagonists, omeprazole, and antacids and those having liver abnormalities, psoriasis, hyper sensitivity to imidazoles or azoles, pregnancy and those lactating were not included in the study group.

(B) Microbiological methods

Nail clipping, and subungual debris were seen under 'KOH' mount preparation. Cultures were done on SDA with chloro and SDA with actidione and incubated at 25°C for 6 weeks.

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Culture positive samples were identified by colony morphology and LCB mount.

(C) Pulse therapy and evaluation of patients

Pulse therapy

Itraconazole was given in a dose of 200 mg b.i.d. for the 1st week followed by 3 week drug-free period, for 1st 3 months for the finger nail cases and 4 months for finger nail + toe nail and toe nail cases.

Evaluation of patients, Patients were evaluated with pulse - dose regimen. Patient evaluation at baseline, week 4, week 8, week 12, week 16, week 24 upto 12 months and assessed for onycholysis, hyperkeratosis, discolouration, nail growth, KOH exam, culture. Evaluated as cleared or markedly improved with clinical success and mycological success (Table II).

Results

Among the study group of patients distribution of sex and age demograph was males 60% (18/30) and females 40% (12/30) with a

Table I. Age and sex incidence (n=30) of patients in study group

Age in years	Male (n=18)				Female (n=12)		
	F.N.*	FN+TN**	T.N.***	F.N.	FN+TN	T.N.	
20-30	3	1	2	0	1	0	
30-45	6	2	3	1	4	1	
45-60	6	3	1	2	4	0	
60	3	0	2	1	3	2	
Total (n=30)	18	6	8	4	12	3	
		18				12	

* F.N. - Finger nail
 ** F.N.+T.N.- Finger nail and toe nail
 ***T.N.- Toe nail

mean age of 45 years. Mean duration of presentation of onychomycosis was 3 years.

Mycological results

At baseline onychomycosis could be proven in all the patients by microscopic evaluation and 60% (18/30) had culture positive infections. Two-thirds 66% (12/18) of the pathogens isolated by culture were dermatophytes, with *Trichophyton rubrum* followed by *T mentagrophytes*. Yeasts were found in 10% of positive culture and 24% pathogens were non-dermatophyte moulds (*Aspergillus* sp and *scopuloriopsis*). Mycological examination at the final visit showed 85% cure rate by microscopy (KOH mount) and absolute cure in culture examination.

Clinical results

After one month 40% of patients showed a clinical response and this was increased to 65% by month 2. On the last follow up visit clinical response was recorded in 90% (27/30) of the patients. Seventy percent completely or ai-

Table II. Evaluation schedule

Month	Month Treatment phase				Follow up phase			
	1st wk 4	2nd wk 8	3rd wk 8	4th wk 12	6th 16wk	8th 24 wk	10th 36 wk	12th 48 wk
Clinical Improvement	NO	mild	good	good	clear	overall success	overall success	overall success
mycological	+++	+++	++	++	+
Mild - 40% nail growth								
Good - 60% nail growth								
Overall Both clinical and mycological.								

most completely got cured (infection remained in a maximum of 10% of nail plate), 15% were markedly and 5% were moderately improved. A relapse type of response was seen in 3 (10%) of patients

Discussion

Itraconazole pulse therapy was well tolerated, by our patients. Side effects were mild

and reported by only 15% of the patients. The most common side effects were gastro-intestinal distress, headache, dizziness and skin problems, mainly pruritus. Andre² observed minor adverse events like headache and gastro-intestinal complaints. In our study 70% cases were completely cured. Excellent compliance was reported with itraconazole pulse therapy regimen in the study of Andre. Odom³ presented three studies of 1-week itraconazole therapy in finger nail and toe nail onychomycosis, showing that this regimen was a significant advance towards achieving patients' and physicians' requirements for treatment. In our study it is observed that itraconazole pulse therapy regimen is more cost effective than continuous therapy. Dubois,⁴ in his study reported that itraconazole pulse therapy yielded the most favourable cost-effectiveness ratio, with the high-

est probability of success compared to itraconazole continuous therapy. In our study we observed that patients preferred itraconazole pulse therapy regimen over a continuous treatment regimen for 3-4 months which is also observed in the study of Andre. Relapse rate in our study was 10% after 12 months of follow up and it was 7% on an average in the study of Andre.²

References

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