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A Comparative Study of Itraconazole and Terbinafine in the Treatment of Onycomycosis

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Abstract

Background: Previous, publications have shown that efficacy and cost of the treatment options to cure onychomycosis. Comparative studies are required to select effective and cheaper drug therapy for the benefit of humankind. Hence current study has been undertaken with an aim to compare efficacy of Itraconazole and Terbinafine on onychomycosis.

Aim: To objectively compare the treatment with Itraconazole and terbinafine in the patients with onychomycosis.

Methods: Randomized, single-blind, longitudinal, clinical retrospective comparative study. Group- A received oral itraconazole 200mg (two capsules of Cap. Sporanoxa 100mg) twice daily for seven consecutive days every month while Group B received oral terbinafine 250 mg (Tab. Sebifina 250mg) twice daily for seven consecutive days every month. The total duration of treatment for both groups was 4 months. The results were calculated statistically using percentages.

***Results*:** 10 (16%) patients in Group A and 12 (20%) patients in Group B were excluded from the analysis of the results as they were not attended for follow up. Of the 50 patients in Group A, 35 (70%) showed clinical cure and 42 (87%) showed mycological cure at the end of one year follow up. In Group B of the 48 patients, clinical and mycological cure were observed in 41 (85%) and 45 (90%) patients respectively. The difference in cure rates between the two groups was not statistically significant (p= >0.05)

Conclusion: Terbinafine pulse therapy is slightly more effective than itraconazole pulse therapy in management of onychomycosis. Further large scale retrospective studies are in need to establish the effectiveness of Terbinafine.

Keywords: Itraconazole, Onychomycosis, Terbinafine

INTRODUCTION

Onychomycosis (OM) - A fungal infection of nail unit caused by dermatophytes, yeasts and non-dermatophyte moulds (NDM).[1] A number of factors contribution for the increase in prevalence of Onychomycosis like age, health problems (diabetes and poor peripheral circulation), Immuno-suppression (due to HIV, use of immunosuppressive drugs, cancer chemotherapy and antibiotics), increased use of commercial swimming pool, occlusive foot wears for exercise and genetic defects that causes alteration in immune function.[2,3,4,5] The prevalence of OM has been reported to be increasing over the years. It affects 3-26% of people worldwide goes to show that it is a significant health problem. Various Indian studies have reported an incidence in the range of 0.5%-5% in the general population.[6, 7] In New Delhi the prevalence of Onychomycosis was confirmed in 45% of the analysed patients.[8]

Management of this disease has improved significantly and treatment patterns have dramatically changed in recent years. Also, newer drugs for OM have improved tolerability profiles compared with older agents. Pharmaco-economic studies help in the decision-making process when selecting the most cost-effective antifungal agents to treat OM. To date there have been a number of national and international studies aimed at effectively assessing the efficacy and cost of the treatment options available to cure OM. Hence, the current study has been undertaken with an aim to compare efficacy of Itraconazole and Terbinafine on OM.

MATERIALS AND METHODS

A Randomized, single-blind, longitudinal, clinical comparative study was under taken in the department of dermatology, Maharajah Institute of Medical Sciences, Nellimarla, during the period from February -2009 to march-2010.

A total of 325 patients were included in the current study after screening from all the patients attended to the OPD of dermatology with clinical feature of Onychomycosis, during the study period.

Exclusion Criteria: Patients with nail abnormalities due to associated skin disease or any systemic disease like psoriasis, lichen plants, contact dermatitis, congenital nail dystrophy malnutrition, iron deficiency, etc., were excluded from the study.

The screening was done by direct microscopic examination of nail material under potassium hydroxide (KOH) examination and culture in Sabouraud's Dextrose agar (SDA).

A baseline liver function test was done in all 325 patients and those with hepatic dysfunction in the form of jaundice and / or elevated hepatic enzymes more than twice the normal values were excluded from the study. Other criteria for exclusion were pregnancy, lactation, concomitant therapy with drugs having a possible interaction with Itraconazole, age < 15 years or > 60 years, and mycologically negative cases (both negative for KOH examination and culture on Sabouraud's dextrose agar (SDA). Total, 120 (72 males and 48 females) patients

satisfied the above criteria were taken for the current study, between the age group of 15-60 years.

All patients were assigned individual identification numbers and were divided randomly and equally into two groups (A and B) using a table of random numbers.

Thus, two groups of 60 patients each with 36 men and 24 women in the age group 15-60 were created. Group A received oral itraconazole 200mg (two capsules of Cap. Sporanoxa 100mg) twice daily for seven consecutive days every month while Group B received oral terbinafine 250 mg (Tab. Sebifina 250mg) twice daily for seven consecutive days every month. The total duration of treatment for both groups was 4 months. The cost of therapy was borne by the patients. The drugs were bought by the physician and dispensed to the patients in unmarked packets containing the entire dosage for seven days every month for four months.

The patients were evaluated at the start of the therapy and thereafter at 4- week (or monthly) intervals for 4 months, followed by evaluation at weeks 24, 36 and 48. During these visits, they were assessed for growth of a normal and healthy appearing nail plate and asked for any adverse effects of the drugs. In addition, microscopic examination of nail material under KOH examination and culture of nail material in SDA was done at 16 weeks and 48 weeks. A liver function test was done twice for all patients at 6 month intervals from the start of therapy.

Clinical cure was defined as replacement of greater than 70% of the mycotic nail bed and plate by normal and healthy appearing nail bed and plate, while any growth less than this was considered as treatment failure. Mycological cure was defined as negative microscopy under KOH examination and a negative culture in SDA at the end of the follow up period. At the end of the study, the results were compiled, tabulated and analyzed using suitable statistical tools like percentage and chi-square tests.

Age in Years	Cases	F	%	T	%	Total (F + T)	Total %
15-30	14 (8/6)	2 (1/1)	14 (12.5/16)	4 (3/1)	28 (37.5/16)	8 (4/4)	58 (50/68)
31-45	27 (17/10)	7 (4/3)	26 (23/30)	7 (6/1)	26 (35/10)	13 (7/6)	48 (42/60)
45-60	19 (11/8)	4 (2/2)	21 (18/25)	7 (4/3)	37 (36/37.5)	8 (5/3)	42 (46/37.5)
Total	60 (36/24)	13 (7/6)	22 (19/25)	18 (13/5)	30 (36/20)	29 (16/13)	48 (45/55)

F=Finger nail involvement**; T=**toe nail involvement

Table: 1 Distribution of total Cases (Male/Female) in Group-A (Itraconazole)

Age in Years	Cases	F	%	T	%	Total (F + T)	Total %
15-30	16 (10/60	5 (3/2)	31 (30/33)	4 (3/1)	25 (30/17)	7 (4/3)	44 (40/50)
31-45	28 (16/12)	7 (5/2)	25 (31/17)	8 (4/4)	29 (25/33)	13 (5/6)	50 (44/50)
45-60	16 (10/6)	4 (3/1)	25 (30/17)	6 (3/3)	38 (30/50)	6 (4/2)	38 (40/33)
n=60	60 (36/24)	16 (11/5)	27 (31/21)	18 (10/8)	30 (28/33)	26 (15/11)	43 (41/46)

F=Finger nail involvement; **T=**toe nail involvement

Table: 2 Distribution of total Cases (Male/Female) in Group B (Terbinafine)

Mycological isolate in SDA	No. of Cases Group A (Itraconazole)	No. of cases Group B (Terbinafine)
Dermatophytes (T. rubrum,T. mentagrophytes)	36 (60%)	39 (65%)
Yeasts (Candida Species)	14 (23%)	11 (18%)
Molds (Aspergillus or Scopulariopsis species)	10 (17%)	10 (17%)

Table: 3 Results of Mycological Study of Specimens

RESULTS:

In the Itraconazole group (A) we observed 70% of cure in which 40% were male and 30% were female. In the Terbinafine group (B) the corresponding figures were 85% of which males were 48% and 37.5% were female.

Microbiological study of the nail material by culture in SDA with chloramphenicol showed growth of dermatophytes, molds and yeasts. The commonest isolates in culture were dermatophytes, i.e., Trichophyton rubrum and Trichophyton mentagrophytes, seen in 60% and 65% of isolates in Groups A and B respectively. Yeasts (Candida spp.) were seen in 23% of Group A and 18% of Group B isolates. Molds like aspergillus and scopulariopsis were observed in 17% of isolates of both Group A and Group B.

During the course of the study, 10 (16%) patients in Group A and 12 (20%) patients in Group B could not complete the one year follow up period and were excluded from the analysis of the results. Of the 50 patients in Group A, 35 (70%) showed clinical cure and 42 (87%) showed mycological cure at the end of one year follow up. In Group B of the 48 patients, clinical and mycological cure were observed in 41 (85%) and 45 (90%) patients respectively. The difference in cure rates between the two groups was not statistically significant.

Weeks of follow up	Group A (Itraconazole)		Group B (Terbinafine)	
	No of cases 50	%	No of cases 48	%
Week 4	0	0%	0	0%
Week 8	0	0%	0	0%
Week 12	0	0%	0	0%
Week 16	1	2%	2	4%
Week 24	15	30%	24	50%
Week 36	26	52%	34	70%
Week 48	35	70%	41	85%

Table: 4 Evaluation schedules of Patient with both Drugs

Adverse effects were seen in 9 (18%) patients on itraconazole (gastric upset. 4; taste disturbance, 3; headache, 1; and jaundice, 1) and in 11 (22%) in the Terbinafine group (gastric upset, 5; headache, 2; maculopapular rish, 2; and altered taste, 2). None of these effects was significant enough to discontinue therapy except in one patient on itraconazole who developed jaundice in the middle of the third pulse. In this patient itraconazole was discontinued and other hepato-protective agents were given in consultation with the gastroenterology department. Within a month the patient was perfectly healthy without any sequelae.

The cost of the 4 pulse regimen of Terbinafine was Rs.2250 (approx.) and that of Itraconazole was Rs.5600 (approx.)

DISCUSSION

Until a few years ago, griseofulvin and ketoconazole were the only 2 oral agents available for the treatment of dermatophyte onychomycosis. With the availability of the newer antifungal agents, such as itraconazole, Terbinafine, the armamentarium of drugs available to treat onychomycosis has expanded. The objective of this study was to determine the efficacy and relative cost effectiveness of the most commonly used oral antifungal agents in the treatment of dermatophyte onychomycosis of the toenails. The time horizon was 1 year. First, the purpose of the study, the comparator drugs and their dosage regimens were defined. The medical practice and resource-consumption patterns associated with the treatment of onychomycosis were identified a meta – analysis was performed on all studies meeting prespecified criteria, and the mycological cure rates of the comparator drugs were determined.

CONCLUSION

Terbinafine pulse therapy is slightly more effective than itraconazole pulse therapy in treating onychomycosis. We have shown that with the availability of Terbinafine and itraconazole, both drugs are well tolerated and highly effective, but Terbinafine is therapeutically superior. As per the Indian economic status regimen of Terbinafine is cheaper than itraconazole hence ensuring the patients are more likely to complete the therapy.

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