IJBPAS, October, 2020, 9(10): 2740-2747

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

STUDY ON CLINICAL OUTCOME OF ORAL TERBINAFINE AND ORAL ITRACONAZOLE USED IN ONYCHOMYCOSIS PATIENTS

MUKUNDAN C[1*] AND RUKZAR FATHIMA A[1], SARAVANA KUMAR RT[2] AND KANNAMBAL K[3]

1: Department of Pharmacy, Annamalai University, Annamalai Nagar-608 002

2: Assistant Professor, Department of Pharmacy, Annamalai University, Annamalai Nagar-608002

3: Associate Professor, Department of Dermatology, Venerology and Leprosy (DVL), Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalai Nagar-608 002

***Corresponding Author: C. Mukundan: E-Mail: mukundan1603@gmail.com; Ph. No.: 9597543221**

Received 26th March 2020; Revised 27th April 2020; Accepted 19th May 2020; Available online 1st Oct. 2020

https://doi.org/10.31032/IJBPAS/2020/9.10.5253

ABSTRACT

Background: Onychomycosis is a chronic fungal infection of nail units. It is not only caused by dermatophytes. It also caused by yeasts and non-dermatophyte molds.

Aim: To compare the effectiveness of oral terbinafine and oral itraconazole used in the Management of onychomycosis using onychomycosis severity index (OSI) scoring.

Materials and method: A prospective observational study was conducted in the department of dermatology, venereology and leprosy (DVL) at Rajah Muthiah Medical College & Hospital (RMMCH) over a period of six months from November 2018 to April 2019. The data was collected from 50 patients using a specially designed data collection form. Patients were selected based on inclusion and exclusion criteria.

Results and discussion: A total of 50 patients were included in this study. They were separated into two treatment Groups (A and B), each group had 25 patients. In group A patients receiving terbinafine and in group B patients receiving itraconazole as a treatment. Among these patients,

males (66%) were more affected than females (34%). Before starting treatment, in group A 52% of patients had severe onychomycosis, whereas 32% and 16% were affected with mild to moderate onychomycosis. In group B 40% of patients had severe onychomycosis, whereas 36% and 24% were affected with mild to moderate onychomycosis. After treatment, in group A 76% were cured and 24% were the mild stage, and in group B, 64% were cured and 36% were in mild stages.

Conclusion: This study concludes that terbinafine is more effective than itraconazole in the management of onychomycosis.

Keywords: Onychomycosis, Terbinafine, Itraconazole, onychomycosis severity index

INTRODUCTION

Onychomycosis is a fungal infection of the finger nails or toe nails commonly caused by dermatophytes; it is called *tinea unguium* **[1]**. Typically, onychomycosis presents as a white or yellowish-brown discoloration of the nail **[2, 3]**. Violaceous, green, and black discoloration of the nail plate has also been observed **[2, 4]**. Other clinical manifestations include subungual hyperkeratosis, separation of the nail from the nail bed (onycholysis), and thickening of the nail plate (onychauxis) **[3, 4]**. The term onychomycosis comprises not only the fungal infection but the yeasts and saprophytic molds infection as well. Onychomycosis can affect both toe nails and fingernails, but onychomycosis of the toenail is much more prevalent **[1, 5, 6]**. Men are more affected due to more frequent nail damage from sports and leisure activities **[7]**. Toe nails are about seven to ten times more frequently affected than fingernails due to theirs lower growth rate **[8, 9]**. The big toenails are most often affected **[2]**. Walking in barefoot, wearing unfitted or the wrong size shoes, nail-biting (onychophagia), and dealing with chemicals can further lead the patients to infection **[10]**. Risk factors include aging, diabetes, tine pedis, psoriasis, immune disorders, and close contact with persons who have onychomycosis **[11, 12]**. Treating onychomycosis is disappointing because clinical outcomes of available antifungal therapy is poor, longer treatment period, high treatment cost **[13]**. However, the arrival of terbinafine and itraconazole has reformed the onychomycosis treatment because these drugs have high cure rates **[9, 14]**. For severe onychomycosis, Oraltherapy is the most effective therapy when compared with topical antifungal treatment and antifungal nail lacquers **[15-17]**. In this study, we compared the effectiveness of oral

terbinafine and oral itraconazole for the treatment of onychomycosis.

MATERIAL AND METHOD

Study design:

A prospective observational study was conducted in the department of dermatology venereology and leprosy (DVL) at Rajah Muthiah Medical College Hospital, Annamalai University which is 1400 bedded multi-specialty tertiary care teaching hospital located in Annamalai Nagar, Chidambaram, Tamil Nadu, India from the period of November 2018 to April 2019.

Selection criteria:

Inclusion criteria:

Patients of both gender and age 18 years above, who attending the outpatient clinic or admitted to the DVL ward with the diagnosis of onychomycosis.

Exclusion criteria:

Patients who are aged 18 years below, pregnant and lactating women, and the patient who are not willing to participate.

Fifty patients, who fulfilled the selection criteria were included in the study. They were randomly allocated into two treatment groups. Patients in group A receiving terbinafine as treatment and patients in group B receiving itraconazole as a treatment.

Treatment:

Doses given to the patient were as follows: terbinafine (7.5 mg/kg/day) and itraconazole (5mg/kg/day). Patients were asked to bring used medicine strips at each visit. They were recommended to take the medicines as prescribed at each visit and received the treatment for 8 weeks or cure. Which one occurs earlier.

Follow up:

Patients were followed up at 2 weekly intervals up to 8 weeks or cure which one occurs earlier.

Clinical assessment:

At each visit, clinical response to the treatment was monitored by observing the area of involvement, theproximity of the disease to the matrix and the presence of longitudinal streaking or patch (dermatophytoma) or subungual hyper-keratosis by using onychomycosis severity index scoring.

Onychomycosis severity index (OSI) consisting of grading the percentage of plate involvement, the proximity of infection to the matrix, degree of subungual hyperkeratosis and presence of dermatophytomo.

To access the severity, the score of the area of involvement range from 0 to 5 is multiplied with the score of the proximity of disease to the matrix range from 1 to 5 and

then add 10 points ifs longitudinal streak or patch (dermatophytoma) is present or if there is greater than 2 mm of subungual hyperkeratosis **(Table 1)**. A total score of 0 indicates cured; 1 through 5 indicates mild; 6 through 15 indicates moderate; and 16 through 35 indicates severe onychomycosis **[18]**.

The study was endorsed by the Institutional Human Ethics Committee (IHEC) prior to the commencement of the study. The IHEC approval letter number is IHEC/0392/2018. All patients gave informed consent form before they were included in the study.

RESULTS

A total of 50 patients with onychomycosis were included in the study. It is found that onychomycosis can affect people of all ages and both the genders. The demographic data shows that among these 50 patients, 33(66%) were male and 17(34%) were females. About 21(42%) patients were at the age group of 41-50 and 19(38%) patients under the age group of 51-60 and 8(16%) patients under the age of 30-40 and 2(4%) patients under the age group 61-70 **(Table 2)**.

The Severity of the onychomycosis was measured by using onychomycosis severity index scoring. Before starting the treatment, patients in group A receiving terbinafine, 52% of patients had severe onychomycosis, whereas 32% and 16% were infected with mild to moderate onychomycosis **(Table 3)**. Patients in group B receiving itraconazole, 40% of patients had severe onychomycosis, whereas 36% and 24% were infected with mild to moderate **(Table 4)**.

After treatment, patients in group A receiving terbinafine, 76% were cured and 24% were in mild Onychomycosis **(Table 3**). Patients in group B receiving itraconazole, 64% were cured and 36% were in mild onychomycosis **(Table 4)**.

Table 1: Onychomycosis Severity Index

Area of Involvement		Proximity of disease to matrix		Presence of dermatophytoma or subungual hyperkeratosis> 2 mm	
Affected nail, %	No. of points	Amount of Involvement from distal edge	No. of points	Present	No. of points
0	0	<1/4	1	No	0
1-10	1	1/4-1/2	2	Yes	10
11-25	2	>1/2-3/4	3		
26-50	3	>3/4	4		
51-75	4	Matrix involvement	5		
76-100	5				

Table 2: Demographic data of patient (N=50)

PARAMETERS		N(%)
Gender	Male	33(66%)
	Female	17(34%)
Age(in years)	30-40	8(16%)
	41-50	21(42%)
	51-60	19(38%)
	61-70	2(4%)

Table 3: Onychomycosis severity index for group A (N=25)

Severity of onychomycosis	Before treatment N (%)	After treatment N (%)
Cured	0	19(76%)
Mild	8(32%)	6(24%)
Moderate	4(16%)	0
Severe	13(52%)	0

Table 4: Onychomycosis severity index for group B (N=25)

Severity of onychomycosis	Before treatment N (%)	After treatment N(%)
Cured	0	16(64%)
Mild	6(24%)	9(36%)
Moderate	9(36%)	0
Severe	10(40%)	0

DISCUSSION

Till now, treating onychomycosis is one of the biggest challenge for dermatologists. Antimycotic agents like Griseofulvin, it was one of the early antibiotics extracted from *penicillium griseofulvin*. It acts againstthe most dermatophytes (*Epidermophyton, Trichophyton, Microsporum,* etc.), but not against *Candida* and other fungus causing deep mycosis **[19, 20]**.

Ketoconazole also much more effective, but it has the risk of hepatotoxicity will reduces its widespread Use **[21]**. Itraconazole, Fluconazole and Terbinafine are the most commonly used antifungal agents for the treatment of onychomycosis. These fungistatic agents have a better pharmacokinetic profile and has fewer adverse reactions **[9, 14]**.

Terbinafine belongs to a new allylamine class of antifungals. It is a non- competitive inhibitor which inhibits 'squalene epoxidase', an early step enzyme that generates squalene epoxide that is converted to lanosterol and then to ergosterol by fungi. It predominantly effective against fungus and candida, and less active against molds, dimorphic fungi and yeasts. Even after stopping the treatment, it remains in the nail for more than a month.

Itraconazole belongs to the triazole class of antifungals. It has a broad spectrum of activity than ketoconazole or fluconazole; includes few molds like Aspergillus as well. Some fluconazole- resistant Candida are susceptible. It's fungistatic, but effective in

immunocompromised patients. It inhibits a microsomal cytochrome P450-dependent synthesis of ergosterol, which in turn inhibits cell-membrane formation. which leads to the arrest of fungal growth.

The severity of onychomycosis at the baseline and end of the study was measured by onychomycosis severity index (OSI) scoring. At baseline, patients in group A receiving terbinafine, 52% of patients had severe onychomycosis, whereas 32% and 16% were mild to moderate. Patients in group B receiving itraconazole, 40% of patients had severe onychomycosis, whereas 36% and 24% were infected with mild to moderate. After treatment, patients in group A, 76% were cured and 24% were in mild onychomycosis. Patients in group B, 64% were cured and 36% were in mild onychomycosis. Our study shows that both terbinafine and itraconazole achieves similar cure rates, but terbinafine is more effective than itraconazole.

CONCLUSION

Terbinafine was the most effective drug when compared with itraconazole for the treatment of onychomycosis.

ACKNOWLEDGEMENTS

Authors are very thankful to the department of dermatology, venereology, and leprosy (DVL), Rajah Muthiah Medical College Hospital (RMMCH) and the Institutional Human Ethics Committee (IHEC) of Rajah Muthiah Medical College (RMMC) for allowing us to conduct the study.

Funding: no funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional human ethics committee.

REFERENCE

[1] Karaman B, Açıkalın A, Ünal İ, Aksungur V. Diagnostic values of KOH examination, histological examination, and culture for onychomycosis: a latent class analysis. International Journal of Dermatology. 2018; 58(3): 319-324.

[2] Thomas J, Jacobson G, Narkowicz C, Peterson G, Burnet H, Sharpe C. REVIEW ARTICLE: Toenail onychomycosis: an important global disease burden. Journal of Clinical Pharmacy and Therapeutics. 2010; 35(5): 497-519.

[3] Allevato M. Diseases mimicking onychomycosis. Clinics in Dermatology. 2010; 28(2): 164-177.

[4] Lipner SR, Scher RK. Onychomycosis: Clinical overview and diagnosis. J Am Acad Dermatol 2019; 80(4): 835-51.

[5] Haghani I, Shams-Ghahfarokhi M, Dalimi Asl A, Shokohi T, Hedayati M. Molecular identification and antifungal susceptibility of clinical fungal isolates from onychomycosis (uncommon and emerging species). Mycoses. 2018; 62(2): 128-143.

[6] Becker BA, Childress MA. Common Foot Problems: Over-the-Counter Treatments and Home Care. Am Fam Physician. 2018 Sep 01; 98(5): 298-303.

[7] Kashyap B, Bhalla P, Kaur R. Onychomycosis - epidemiology, diagnosis and management. Indian Journal of Medical Microbiology. 2008; 26(2): 108.

[8] Baran R, Hay R, Haneke E, Tosti A, editors. Onychomycosis: The current approach to diagnosis and therapy. London: Informa Healthcare; 2006.

[9] Gupta A, Mays R, Versteeg S, Shear N, Piguet V. Update on current approaches to diagnosis and treatment of onychomycosis. Expert Review of Anti-infective Therapy. 2018; 16(12): 929-938.

[10] Sehgal VN, Srivastava G, Dogra S, Chaudhary A, Adhikari T. Onychomycosis: An Asian perspective. Skinmed 2010; 8: 37-45.

[11] Arsenijević V, Denning D. Estimated Burden of Serious Fungal Diseases in Serbia. Journal of Fungi. 2018; 4(3): 76.

[12] Lipner SR, Scher RK. Onychomycosis: Clinical overview and diagnosis. J. Am. Acad. Dermatol. 2019 Apr; 80(4): 835-851.

[13] Epstein E. How Often Does Oral Treatment of Toenail Onychomycosis Produce a Disease-Free Nail?. Archives of Dermatology. 1998; 134 (12).

[14] Gupta A, Lynde C, Konnikov N. Single-blind, randomized, prospective study of sequential itraconazole and terbinafine pulse compared with terbinafine pulse for the treatment of toenail onychomycosis. Journal of the American Academy of Dermatology. 2001; 44(3): 485-491.

[15] Drago L, Micali G, Papini M, Piraccini BM, Veraldi S. Management of mycoses in daily practice. G Ital Dermatol Venereol. 2017 Dec; 152(6): 642-650.

[16] Lok C. [What's new in clinical dermatology?] Ann Dermatol Venereol. 2016 Dec; 143 Suppl 3: S1-S10.

[17] Wollina U, Nenoff P, Haroske G, Haenssle H. The Diagnosis and Treatment of Nail Disorders. Deutsches Aerzteblatt Online. 2016.

[18] Carney C, Tosti A, Daniel R, *et al*. A New Classification System for Grading the Severity of Onychomycosis: Onychomycosis Severity Index. Arch Dermatol. 2011; 147(11): 1277–1282. doi:10.1001/archdermatol.2011.267

[19] Tripathi K. Essentials of medical pharmacology. 8th ed. New Delhi: Jaypee Brothers; 2019.

[20] Roberts D. Oral therapeutic agents in fungal nail disease. Journal of the American Academy of Dermatology. 1994; 31(3): S78-S81.

[21] Galimberti R, Negroni R, Iglesia de Elias Costa M, Casala A. The Activity of Ketoconazole in the Treatment of Onychomycosis. Clinical Infectious Diseases. 1980; 2(4): 596-598.