

Original Research Article

Therapeutic study of onychomycosis in a tertiary care center

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ABSTRACT

Background: Onychomycosis is the fungal infection of nail unit and require long-term treatment to achieve complete cure. This study aims to know the effectiveness of various treatment protocols for onychomycosis.

Methods: This randomized uncontrolled open label study was undertaken in a tertiary care hospital. Patients with onychomycosis were included. Patients who received systemic or topical antifungal therapy in last six months were excluded. After obtaining ethical approval they were subjected to KOH mount and culture from nail clippings. Patients were selected randomly with both KOH and culture positive. Patients were divided into 3 groups. Group-A received oral terbinafine, Group-B received oral terbinafine and topical amorolfine, Group-C received oral itraconazole and topical amorolfine for 6 months. The patients were evaluated and assessed for the growth of the nail plate and were inquired for any adverse effects due to the drugs, at 6, 12 and 24 weeks. The results were recorded and detailed statistical analysis was done.

Results: During the course of study 9 patients were lost in follow up and were excluded from the analysis of results. Mycological cure with negative KOH microscopy and culture were obtained in 56.6%, 73.3% and 70% in groups A, B and C. Clinical cure was observed in 60%, 76.6%, and 73.3% patients in group A, B and C respectively.

Conclusions: There was no statistically significant difference in cure rate among the different treatment groups. Combination therapy achieved better results compared to monotherapy.

Keywords: Onychomycosis, Treatment, Terbinafine, Itraconazole

INTRODUCTION

Onychomycosis is the fungal infection of the nail bed, matrix or nail plate caused by dermatophytes, non dermatophyte moulds and yeasts.^{1,2} Up to 90% of mycotic nail infections and 50% of finger nail infections are caused by dermatophytes.³ Yeasts causes 5% and non dermatophyte moulds causes 4% of onychomycosis.^{4,5} There are several factors to be considered in the management of onychomycosis like the drug efficacy, dosage, duration and cost along with the patient and disease profile.

The commonly used topical agents for treatment of onychomycosis are 5% amorolfine nail lacquer, 8% ciclopiroxolamine nail lacquer, 28% tioconazole, Bifonazole and 40% urea paste.⁶ Other topical therapies are 1% bifonazole and 40% urea, clotrimazole cream and solution, miconazole tincture, glutaraldehyde 10% solution, 1% fluorouracil in propylene glycol, a tincture containing triacetin, sodium propionate, benzalkonium chloride, cetylpyridinium chloride and chloroxylenol, vitamin E, naftifine hydrochloride 1% gel, topical ketoconazole under occlusion following nail avulsion. Amorolfine is active against dermatophytes and

dimorphic fungi with activity against yeasts and moulds being more variable.¹¹

The systemic agents used are griseofulvin, fluconazole, itraconazole and terbinafine. Griseofulvin is poorly absorbed and has a narrow spectrum with effectiveness extending to dermatophytes only. It is contraindicated in individuals with porphyria, hepatocellular failure and hypersensitivity. Dose of griseofulvin is 500 mg / day 6 months for fingernail onychomycosis and 12 months for toe nail onychomycosis.⁷ Fluconazole has low lipophilicity and proved to be safe and effective in onychomycosis. Dose of fluconazole is 300 mg or 450 mg once weekly for 9 to 12 months.⁸ Itraconazole is effective for dermatophytes, candida and non dermatophyte moulds. It is highly lipophilic, oral bioavailability is maximal when taken with a full meal. Approximately 95% is bound to plasma albumin. It has a high affinity for keratinized tissues and has been detected in distal finger nail material after 1 week of therapy. It persists for upto 6 months after discontinuation of therapy more or less unchanged. Itraconazole can be given as 200 mg once daily for 12 consecutive weeks or as pulse therapy with dose of 200mg twice daily for 1 week every month for 3 to 4 months.⁹ Terbinafine is primarily fungicidal against dermatophytes, aspergillus species, scopulariopsis, blastomyces and histoplasma capsulatum. The activity against yeast is more variable. Terbinafine is well absorbed (>70%) and the bioavailability is 40% as a result of first pass metabolism. Dosage is 250 mg/day for 6 weeks and 12 weeks in fingernail and toenail onychomycosis respectively.¹⁰

Some of the poor prognostic factors in the treatment of onychomycosis includes area of nail involvement >50%, significant lateral disease, subungual hyperkeratosis >2 mm, white, yellow or brown streaks in nail, total dystrophic type, non responsive organisms, patients with immune suppression and diminished peripheral circulation.¹² Recurrence can occur after treatment if proper mycological cure was not achieved.

METHODS

This randomized uncontrolled open label study was conducted in a tertiary care hospital for a period of 18 months. Selection criteria included patients with clinical features of onychomycosis. Among those who received systemic or topical antifungal therapy in the last six months, pregnant, lactating females, those with elevated hepatic enzymes, those not willing for the study were excluded from the drug trial. Ethical approval obtained. They were subjected to detailed history, clinical examination and investigations like KOH mount and culture from nail clippings. 99 patients selected randomly were either both KOH and culture positive and included for study. Patients selected for the study were randomly divided into 3 groups A, B and C. Group A received oral terbinafine 250 mg daily for 6 months, group B received oral terbinafine 250 mg daily and topical amorolfine once

weekly for 6 months, group C received oral itraconazole 200 mg twice daily for one week every month and topical amorolfine once weekly for 6 months. The patients were evaluated at 6 weeks, 12 weeks and 24 weeks. During these visits they were assessed for the growth of the normal and healthy nail plate and were inquired for any adverse effects of the drugs. In addition, microscopic examination and culture of the nail material were done at 12 and 24 weeks. The results were recorded and a detailed analysis was done using SPSS software.

RESULTS

Out of the 99 patients, 37 were male patients and 62 were female patients. The most commonly affected was the 51-60 years age group. 39 patients had fingernail involvement, 17 patients had toe nail involvement and 43 patients had both fingernail and toenail involvement at the time of presentation. Distal and lateral subungual onychomycosis was the most frequent clinical pattern noted in 45 patients followed by total dystrophic type in 29 patients, both DLSO and TDO types in 17 patients (Figure 1), proximal subungual type in 7 patients and superficial white onychomycosis in 1 patient.



Figure 1: DLSO and TDO type of onychomycosis.

On culture of the 99 specimens yeasts and dermatophytes were isolated in 22 and 48 specimens (Figure 2). While non dermatophyte moulds were isolated in 29 specimens.

During the course of study, 9 patients were lost in follow up period and were excluded from the analysis of results. No major adverse effects due to drugs were noted during the study period. At sixth month follow up, the mycological response with KOH mount and culture in the study group noted as shown in Table 1.

The mycological cure rate was 56.6%, 73.3% and 70% in group A, B and C respectively. Clinical cure was noted as the absence of clinical signs of onychomycosis, distal subungual hyperkeratosis or onycholysis leaving less than 10% of the nail plate affected, Clinical cure was observed in 60%, 76.6% and 73.3% of patients in group A, B and C respectively as shown in Table 2.

Table 1: Mycological response in study group (n=30).

Fungal isolate	Group A		Group B		Group C	
	Total	Mycological cure	Total	Mycological cure	Total	Mycological cure
Dermatophytes	16	10	15	11	14	9
Yeasts	6	3	7	5	7	5
Non dermatophytes	8	4	8	6	9	7
Overall response	30	17	30	22	30	21
Overall percentage	56.6%		73.3%		70%	

Table 2: Clinical response in study group.

Group	Total	Clinical cure	Percentage (%)
A	30	18	60
B	30	23	76.6
C	30	22	73.3

**Figure 2: Dermatophyte isolated in culture.**

DISCUSSION

Onychomycosis is known to be a difficult to treat condition and often exerts a significant negative impact on the quality of life. The agents most commonly used for treatment of onychomycosis are oral griseofulvin, fluconazole, itraconazole, terbinafine, topical ciclopiroxolamine and amorolfine. In order to evaluate the superiority of one antifungal agent over another, a lot of comparative studies have been done. Fluconazole wasn't included in most of the studies.

The newer antifungal agents have better pharmacokinetic properties such as prompt penetration of nail bed, persistence in nail for several months and fewer adverse effects. Baran et al, studied the efficacy of a combination therapy with amorolfine nail lacquer and oral terbinafine in comparison to oral terbinafine alone for the treatment of onychomycosis and concluded combination enhances clinical efficacy and is more cost effective.¹³

Honeyman et al have treated 85 patients with itraconazole 200 mg/day and other 82 patients with terbinafine 250 mg/day for 4 months. At the end of the study, clinical

cure rate for terbinafine group was 57.8% and 62.6% for itraconazole group.¹⁴ However in researches with larger number of patients, terbinafine treatment efficacy resulted to be greater than that of itraconazole and this difference was significant.¹⁵ The continuous therapy with terbinafine showed superiority and the relapse rate was very low in comparison with intermittent therapy.¹⁶ For itraconazole the characteristic thing is that its concentration in nail unit remains high even after cessation of therapy.¹⁷ Therefore itraconazole may be administered in pulse therapy regimens once in 4 weeks.

Combination of topical therapy with newer oral antifungal agents may increase the efficacy in onychomycosis treatment and shorten the duration of therapy.^{18,19}

CONCLUSION

Oral terbinafine and itraconazole with topical amorolfine combination therapy gave mycological cure rate higher than terbinafine monotherapy. Combination therapy and pulse itraconazole therapy are cost effective and ensured that the patients are likely to complete the therapy.

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