

RESEARCH ON CLINICAL CHARACTERISTICS AND TREATMENT RESULTS OF DERMATOPHYTOSIS PATIENTS WITH THE COMBINATION OF TOPICAL TERBINAFINE AND ORAL ITRACONAZOLE

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ABSTRACT

Background: Currently, many patients with dermatophytosis are treated with a variety of antifungal drugs but they are ineffective and relapses are common. Many antifungal drugs have been used but fails to treat the disease, which can globally become an issue in medical practice. The combination of antifungal drugs for the treatment of dermatophytosis, including oral itraconazole and topical terbinafine, has been shown to be more effective than monotherapy. However there has not been much research on the effectiveness of this combination treating dermatophytosis in Vietnam. **Objectives:** To describe the clinical characteristics and evaluate the results of patients with dermatophytosis treated with the combination of oral itraconazole and topical terbinafine at Can Tho Hospital of Dermato-Venereology in 2023. **Materials and methods:** a cross-sectional descriptive study was conducted on 53 patients who were diagnosed with dermatophytosis at Can Tho Hospital of Dermato-Venereology from May to November 2023. **Results:** the age group of 16 – 30 years old (47.2%) and male gender (67.9%) were the most common. The dominant clinical characteristics were pruritus (96.2%), erythema (100%), scaling (90.6%), central skin atrophy (88.7%), tinea corporis (90.6%), tinea cruris (28.3%), polycyclic pattern (79.2%) and round pattern (71.7%). The severity scores of the three symptoms and signs (pruritus, erythema and scaling) at the second week and fourth week were significantly decreased, compared with their baseline values ($p < 0.001$). The cure rate of the patients after the second and fourth weeks of treatment were 28.3% and 90.6% respectively. **Conclusion:** pruritus, erythema, scaling, central skin atrophy, tinea corporis, tinea cruris, polycyclic pattern and round pattern were the most common clinical characteristics in dermatophytosis. With the treatment that combined of topical terbinafine and oral itraconazole, symptoms of the disease were significantly reduced.

Keywords: dermatophytosis, itraconazole, terbinafine, clinical characteristics, treatment results

I. INTRODUCTION

Dermatophytosis is a common infection, affecting 20-25% of the global population [1]. Many antifungal drugs have been used but failed to cure the disease. A survey by Saunte et al., showed that in Europe, clinically and/or mycologically antifungal resistance was observed in 17/20 countries [2]. According to Sudip Das et al., *Trichophyton* strains are most sensitive to oral itraconazole [3]. Meanwhile, Dongxin Zhang et al. found that, the combination of terbinafine and itraconazole was significantly more effective than monotherapy with itraconazole or terbinafine [4]. However, studies on these issues have not been done much in Vietnam. Therefore, we conducted this study to evaluate the clinical characteristics and results of dermatophytosis patients treated with the combination of those drugs. There are two objectives in our study:

1. Describe the clinical characteristics of patients with dermatophytes at Can Tho Hospital of Dermato-Venereology in 2023.

2. Evaluating the treatment results of dermatophytosis with the combination of topical terbinafine and oral itraconazole at Can Tho Hospital of Dermato-Venereology in 2023.

II. MATERIALS AND METHODS

2.1. Materials

All patients who went to the hospital and were diagnosed with dermatophytosis at Can Tho Hospital of Dermato-Venereology from May to November, 2023.

Inclusion criteria: Patients who went to hospital and were diagnosed with dermatophytosis and agreed to participate in the study by signing the data collection form. This research was accepted by The Ethics Committee of Can Tho Hospital of Dermato-Venereology.

Exclusion criteria: Female patients who are pregnant, intend to become pregnant or be on breast-feeding, children < 12 years old, have liver and/or kidney dysfunction, are allergic to itraconazole and terbinafine, have HIV infection/myelosuppression/leukemia/organ transplant; who are uncooperative, unable to read and answer questionnaires; or who have tinea capitis.

2.2. Study design: A cross-sectional descriptive study

2.3. Sample size

$$n = \frac{z_{1-\frac{\alpha}{2}}^2 \cdot p(1-p)}{d^2}$$

n: sample size; with $\alpha = 0.05$, $z_{1-\frac{\alpha}{2}} = 1.96$, d: tolerance ($d = 0.075$)

p is the cure rate of dermatophytosis patients treated by oral itraconazole at the end of the 4th week, according to the study by Bhatia et al., which was 91.8% [5].

Minimum n=52. The actual sample size was 53.

2.4. Methods of conducting research

Patients were interviewed and examined by researchers who are currently doctors at the hospital. General characteristics of subjects and clinical characteristics of dermatophytosis were thereby recorded. The patients were then treated with the combined regimen: itraconazole 100 mg orally b.i.d being continued for 2 weeks, in addition to topical terbinafine 1% b.i.d being continued for 4 weeks. Treatment results were evaluated by the researchers at two time points: 2 weeks and 4 weeks after the start of the therapy. Symptoms of pruritus, erythema and scaling were scored at the beginning of treatment, at 2 weeks and at 4 weeks of treatment.

Data were input and analyzed using SPSS 20.0. Descriptive statistics was used to describe the patients general and clinical characteristics. Paired Samples T-Test was used to compare the severity scores of the disease at baseline and when the patients were being treated (weeks 2 and 4).

III. RESULTS

From May to November 2023 at Can Tho Hospital of Dermato-Venereology, 53 patients were included in this study with the following characteristics:

3.1. Age and gender

The age of the included patients ranged from 16 to 61 years (median 32). The 16 - 30 age group accounted for the majority of our study population (47.2%). Meanwhile, the proportion of patients >60 years was the lowest (1.9%). Most patients were men (67.9%).

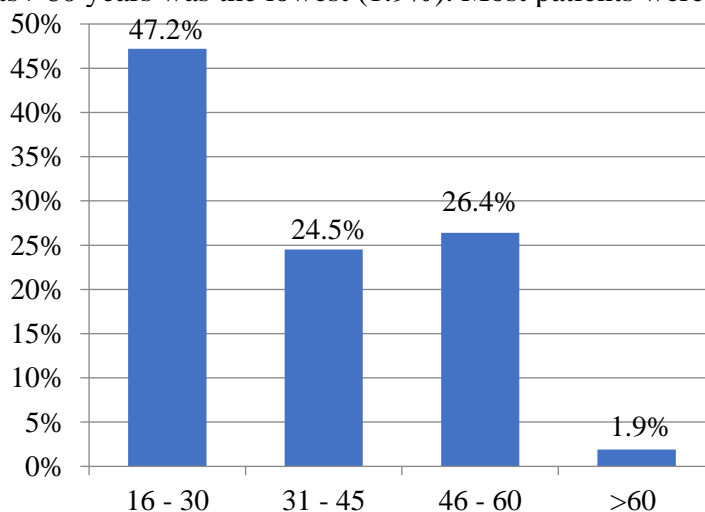


Figure 1: The distribution of age

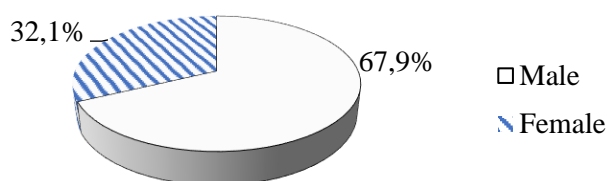


Figure 2: The distribution of gender

3.2. Physical symptoms

Table 1. Symptoms of patients

Symptoms	Yes		No	
	n	%	n	%
Pruritus	51	96.2	2	3.8
Burning	22	41.5	31	58.5
Pain	8	15.1	45	84.9
Others	6	11.3	47	88.7

The symptom with highest proportion was pruritus (96.2%).

3.3. Clinical types of the lesion

Table 2. Clinical types of lesions

Clinical types	Number	Percentage (%)
Tinea corporis	48	90.6
Tinea cruris	15	28.3
Tinea manuum	3	5.7
Tinea pedis	2	3.8
Tinea faciei	6	11.3
Others	1	1.9

The most common clinical type is tinea corporis (90.6%), followed by tinea cruris (28.3%).

3.4. Shapes of lesion

Table 3. Distribution of the shapes of lesion

Shapes of lesion	Number	Percentage (%)
Round	38	71.7
Polycyclic	42	79.2
Others	20	37.7
Total	53	100

The polycyclic pattern was observed in the majority of patients (79.2%), followed by the round pattern (71.7%).

3.5. Signs of the disease

Table 4. Signs of the disease

Signs	Yes		No		Total	
	n	%	n	%	n	%
Erythema	53	100	0	0	53	100
Scaling	48	90.6	5	9.4	53	100
Vesicles, bullae and pustules	19	35.8	34	64.2	53	100
Central skin atrophy	47	88.7	6	11.3	53	100

Erythema occurred in all patients (100%), while vesicles, bullae and pustules were the least common (35.8%).

3.6. Severity scores of common symptoms and signs according to the weeks of treatment

Table 5. Severity scores of common clinical symptoms and signs according to weeks of treatment

Symptoms and signs	Baseline	Weeks of treatment			
		Week	Scores after treatment	Score reduction (%)	P
Pruritus	2.19±0.12	2	0.26±0.08	87.9%	<0.001
		4	0.15±0.07	93.1%	<0.001
Erythema	1.89±0.12	2	0.72±0.08	61.9%	<0.001
		4	0.15±0.07	91.9%	<0.001
Scaling	1.40±0.11	2	0.30±0.08	78.1%	<0.001
		4	0.09±0.06	93.0%	<0.001

Scores of pruritus, erythema and scaling at weeks 2 and 4 were significantly decreased, compared with the baseline values (p<0.001).

3.7. Levels of lesion clearance according to the weeks of treatment

At the 2nd week, the reduction group was the highest (68.9%), and non-response group was the lowest (1.9%). At the 4th week, the cured group was the highest (90.6%) and non-response group was the lowest (3.8%).

Table 6. Levels of lesion clearance according to treatment weeks

Weeks	Levels of lesion clearance					
	Cure		Reduction		Non-response	
	n	%	n	%	n	%
2	15	28.3	37	68.9	1	1.9
4	48	90.6	3	5.7	2	3.8

IV. DISCUSSION

4.1. Age and gender

In our study, the age group 16 – 30 and male gender accounted for the largest number of patients, 47.2% and 67.9% respectively. These results are similar to the study by Satyendra et al. that involved 275 Indian patients [6] of whom the most common age group was 21-30 (36.4%) and of whom 74.1% were male. It is possibly that these groups of age and gender are more active and work more; thus, they sweat more and are more susceptible to fungi.

4.2. Physical symptoms

Regarding symptoms, pruritus was the most prevalent (96.2%). This result is similar to the study by Pham Van Tuan (2021) in Bac Ninh [7] that 100% of patients had pruritus. Dermatophytes may penetrate the stratum corneum, weaken the skin's protective barrier and stimulate the body's immune response, causing the release of chemical mediators, which leads to pruritus and burning sensation.

4.3. Clinical types of the lesion

Regarding the distribution of the clinical types of lesions, tinea corporis accounted for the highest proportion (90.6%), followed by tinea cruris (28.3%). These findings are similarly found by Soodan et al. in India [8]. This could be explained by the fact that tinea corporis and tinea cruris are favorable locations for sweat accumulation, which facilitates the growth of fungi (armpit, groin, inframammary folds, buttocks, back,...).

4.4. Shapes of lesion

Regarding the distribution of lesion shapes, the polycyclic pattern accounted for the highest proportion, 79.2%. This result is similar to that of Le Huynh Phuc (2019) in Binh Thuan [9], being 83.7%. The polycyclic pattern is a very common feature in dermatophytosis, and so is in other dermatoses. Remarkably, it can easily confuse in diagnosis.

4.5. Signs of the disease

Regarding the distribution of signs, all patients had erythema; meanwhile, scaling and central atrophy accounted for most cases, 90.6% and 88.7% respectively. The portion of patients with vesicles, bullae and pustules was however much lower, 35.8%. Our results are similar to the study by Nguyen Thai Dung (2016) in Nghe An [10] with erythema being prevalent in 98.3% of patients, scaling 98.3%, and central skin atrophy 85.3%. According to Fitzpatrick, the classic presentation involves annular or serpiginous plaque with scale across the entire active erythematous border, which may be vesicular, and advances centrifugally. The center of the plaque is usually scaly but may exhibit complete clearance [11].

4.6. Severity scores of the common symptoms and signs according to weeks of treatment

In our study, pruritus, erythema and scaling severity scores were all decreased with statistical significance over each assessment (at the 2nd week and 4th week). On the other hand, the study by Bhatia et al. [5], examined the monotherapy of itraconazole, showing that at 2nd week, the score of pruritus was 1.18 ± 0.62 , erythema 0.66 ± 0.66 , and scaling 1.04 ± 0.44 ; At 4th week, the respective values were 0.16 ± 0.48 , 0.19 ± 0.65 , and 0.16 ± 0.48 . Compared with Bhatia et al., our severity scores at the 2nd week and 4th week were much lower, even though our baseline scores were higher. This suggests the effectiveness of combining oral itraconazole and topical terbinafine.

4.7. Levels of lesion clearance according to weeks of treatment

The cure rate at 4th in our study week is lower than that of Zhang et al. [4], 90,6% vs. 100%. Otherwise, the study by Bhatia et al. [5] showed that monotherapy of itraconazole attained complete lesion clearance of 0.02% and a reduction rate of 58% at the end of the 2nd week, which were lower than those of our study. However, at the end of the 4th week, their complete lesion clearance (91.8%) was similar to our results. This shows that the combination of oral itraconazole and topical terbinafine can help improve the disease faster than using itraconazole alone.

V. CONCLUSION

Pruritus, erythema, scaling, central skin atrophy, tinea corporis, tinea cruris, polycyclic pattern and round pattern are the most common clinical characteristics in dermatophytosis. By combining oral itraconazole and topical terbinafine, our study showed that symptoms of this disease were significantly reduced.

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