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Oral Itraconazole and Terbinafine vs. Itraconazole as a Novel Regimen for the Newly Emergent Chronic Tinea: A Comparative Clinical Study

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Abstract

Dermatophytosis is the most common contagious fungal disease. Iraq, like many other countries around the world, is facing the emergence of chronic, resistant, and relapsing tinea infections. This study compared the efficacy, safety, and relapse rate of a combination therapeutic regimen of itraconazole and terbinafine vs. itraconazole alone in the treatment of chronic tinea infections. Patients were divided equally into two groups. Group I received a combination of itraconazole and terbinafine, while group II was on itraconazole alone for eight weeks for each group. For the assessment of the relapse rate, follow-up was for two months. Only 148 out of 160 enrolled patients completed the study. 98 (66.2%) were males, and 50 (33.8%) were females. The mean age (±SD) of the total was 33.04±12.65 years. There was no significant difference in their residency. Family history was positive in the majority of patients 119 (80.4%). After two weeks, there was a significant difference in response to treatment between the two groups (p value < 0.00), with a marked clearance achieved by 54 (73%) patients in group I and only 17 (23%) patients in group II. After 8 weeks, complete clearance was 68 (92%) in group I and 35 (47%) in group II; marked clearance was 6 (8%) in group I and 33 (45%) in group II. 6 (8%) patients in group II still have incomplete clearance. The relapse rate after 16 weeks was 5 (7%) in group I and 42 (57%) in group II (p value < 0.00). In conclusion, therapeutic regimens of itraconazole and terbinafine were effective, safe, and well tolerated, with a low relapse rate.

Keywords: Antifungal, Chronic dermatophytosis, Itraconazole, Terbinafine.

Introduction

Dermatophytosis is the most common contagious fungal disease among superficial mycosis [(1)]. It is also called tinea infection and is caused by dermatophytes, which are fungi that invade, multiply, and feed on keratinized tissues like nails, hair, and skin [(2)]. They are filamentous fungi [(3)], which are divided into three genera: *Epidermophyton, Microsporum,* and *Trichophyton.*

In humans, the most common isolate is *Trichophyton rubrum*, followed by *Trichophyton mentagrophytes* [(4)]. The high incidence of *Trichophyton rubrum* clears in Europe, whereas the incidence of *Trichophyton mentagrophytes* was higher in Asia [(5)]. Dermatophytes are classified according to the mode of transmission: geophilic, zoophilic, and anthropophilic. They are clinically categorized into tinea corporis, which specifies infection of the limbs or trunk; tinea cruris indicates infection of the groin; tinea unguium (nails); tinea pedis (foot); tinea manuum (hand); tinea barbae (beard); tinea faciei (face); and tinea capitis (head) [(6)]. An increasing prevalence of dermatophytosis across the world has been seen in previous years, especially in the tropics [(7)]. Warmth and moisture are the most important factors contributing to the wide distribution of superficial dermatophytosis in tropical countries [(5)].

A change in epidemiology may be attributed to the outbreak of a recent increase in the prevalence, chronic, relapsing, and resistance of dermatophytosis, especially in India, Iran, Syria, and our country, Iraq. Recently, Iraq has faced a wide spread of chronic, relapsing, and resistant attacks of superficial dermatophytic infection in different provinces like Baghdad, Anbar, Thi-Qar, Wasit, Babylon, Karbala, Diwania, and Najaf in a way that has never been encountered before [(8-16)]. *Trichophyton rubrum* and *Trichophyton mentagrophytes*, followed by *Microsporum canis*, were the main etiological agents [(17)].

The diagnosis of dermatophyte infections is based on medical history and clinical observation supported by potassium hydroxide (KOH) microscopy. KOH aids in confirming the diagnosis of dermatophytosis.

A scale is obtained from the active border of the lesion with a scalpel blade then put on a glass slide and added with a few drops of 10% KOH. Examine under a microscope (×400) for visualization of hyphae [18]. The gold standard of diagnosis is the culture, but it has low sensitivity and takes a long time [18-19].

Itraconazole from the triazoles group and terbinafine from the allylamines group are used as oral therapies for dermatophytosis. The cell membrane is the same biological target for the action of both itraconazole and terbinafine. Sterol 14-α-demethylase is inhibited by itraconazole, and squalene epoxidase is inhibited by terbinafine, both of which prevent the formation of ergosterol. Additionally, allylamines promote the buildup of lanosterol, a hazardous intermediate substance in the ergosterol production pathway [20-22]. Many studies compared the combination of itraconazole and terbinafine vs. itraconazole or terbinafine alone [23-27].

An emergence of clinical resistance to the traditional treatment with antifungals like terbinafine-resistant mycoses has been observed as a major concern, especially in areas like Iraq [9, 28]. Synergistic effects of two or more antifungal drugs are a well-known idea to handle possible drug resistance while enhancing treatment efficiency [29]. This study was designed to compare the efficacy, safety, and the relapse rate of a combination therapeutic regimen of itraconazole and terbinafine vs. itraconazole alone in the treatment of chronic tinea corporis and/or tinea cruris infections.

Patients and Methods

This comparative study was conducted for patients with chronic tinea at the dermatology and venereology outpatient's unit, Ramadi Teaching Hospital, and the department of dermatology, College of Medicine, University of Anbar, Iraq, during the period between May 2022 and May 2023, after obtaining approval and permission from the Anbar Health Directorate, Center of Training and Human Development, Research Committee (Ref. No. 2022041 dated May 29, 2022). A written informed consent was obtained voluntarily by the patients after explaining the clinical study protocol and describing the risks and benefits in detail.

Patients of both sexes who were older than 18 years old with chronic tinea corporis, tinea cruris, or both were eligible for this study. Chronic cases were defined as those who had the illness for longer than three months (greater than 12 weeks), with or without a history of therapy [30]. Cases were diagnosed clinically by a dermatologist and supported by a positive KOH examination.

Patients who had terbinafine or itraconazole hypersensitivity, as well as those who had recently received systemic oral antifungal therapy within the previous month, pregnant and lactating women, immunocompromised status, presence of any other chronic disease requiring systemic therapy, including cardiac disease, diabetes, or Cushing's syndrome, and abnormal results in liver function tests (LFT), complete blood counts (CBC), and renal function tests (RFT), were excluded from the research. All female patients who were of reproductive age were advised to avoid pregnancy. Individuals suspected to have chronic dermatophytosis (chronic tinea corporis and/or tinea cruris) were designated for KOH examination of skin scrapings, which were collected from them after referral from the dermatologist in charge.

Depending on the mode of therapy, patients with positive chronic tinea infections were divided into two groups: a combination of itraconazole and terbinafine (group I) or itraconazole alone (group II). These groups were then compared and graded as follows:

- Group I: patients treated by oral itraconazole 100 mg twice daily in a combination with terbinafine 250 mg once daily for two months.
- Group II: patients treated by oral itraconazole 100 mg twice daily for two months.

Itraconazole was recommended to be taken with a meal to ensure maximum absorption, as well as to avoid H2 receptor antagonists and antacids during the treatment. The follow-up period was eight weeks for both groups. At the baseline visit (1st visit), all patients provided pertinent clinical information such as age, sex, sites of involvement, residence, and family history. The clinical type and morphology of lesions were provided by dermatologists. A physical examination and mycological examination (microscopy) were carried out, as were clinical laboratory assessments for LFT before and at the end of management for evaluating the side effects of itraconazole.

The second, third, fourth and fifth visits were after two, four, six, and eight weeks, respectively for assessments of efficacy and safety. Patients were recommended not to take any medication other than the indicated antifungal agents. During the follow-up period (two months), patients returned monthly for assessment of the presence or absence of relapse. Relapse was defined as the appearance of previous or new lesions during the follow-up period.

For the assessment of treatment efficacy, two variables were considered:

1. Mycological cure: microscopy negative performed at the end of the treatment course.
2. Dermatologist's clinical evaluation for symptoms assessments (erythema, hyperpigmentation, desquamation, and pruritus were considered the target symptoms).

The evaluation of overall success (mycological and clinical) in response to treatment was as follows [2, 10]:

A. Complete clearance: microscopy negative, clearance of all target symptoms.
B. Marked clearance: microscopy negative; hyperpigmentation; no desquamation; no erythema; no pruritus.
C. Incomplete clearance: microscopy positive, hyperpigmentation, no desquamation, no erythema, no pruritus.
D. No change: microscopy positive, presence of all target symptoms.
E. Worsening.

The safety of treatment is also noted by the assessment of adverse effects, with special attention paid to serious or severe adverse events leading to withdrawal. The collected data was entered in SPSS version 22. A non-parametric Mann-Whitney T-test and Chi-square test were applied to test the hypothesis. The P-value ≤ 0.05 was considered significant.

Results

A total of 160 patients were enrolled in this comparative study. For unknown reasons, 12 patients lost follow-up. 148 patients completed the duration of treatment (2 months) and were divided equally (74 patients) into each group. At baseline (1st visit), demographic characteristics are obtained from all enrolled patients (Table 1). Among them, 98 (66.2 %) were males and 50 (33.8%) were females. Males in group I were 42 (42.9%) and in group II were 56 (57.1 %), while females were 32 (64%), 18 (36%), in groups I and II, respectively. The mean age (±SD) of all patients was 33.04±12.65 years, while it was 31.76±12.6 years in group I and 34.32±12.65 years in group II. There was no significant difference (P value 0.09) in the mean age between the two groups. Their residency was 70 (47.2%) in urban areas and 78 (52.8%) in rural areas. Family history was positive in the majority of patients, 119 (80.4%), while only 29 (19.6%) have a negative family history. Tinea corporis was 58 (39.2%), tinea cruris was 33 (22.3%), and both types (Corporis and Cruris) were 57 (38.5%).

Table 1. Baseline (1st visit) demographic characteristics of enrolled patients

Data	**Total** N (%)	**Croup I** (Itraconazole & Terbinafine) N (%)	**Group II** Itraconazole alone N (%)	***P*-value** (between two groups)
Number of Patients	148	74 (50)	74 (50)	
Sex Male Female	 98 (66.2) 50 (33.8)	 42 (42.9) 32 (64)	 56 (57.1) 18 (36)	 0.01
Age (years) (Mean±SD)	33.04±12.65	31.76±12.6	34.32±12.65	0.09
Residence Urban Rural	 70 (47.2) 78 (52.8)	 24 (34.3) 50 (64.1)	 46 (65.7) 28 (35.9)	 < 0.00
Family History Positive Negative	 119 (80.4) 29 (19.6)	 68 (57.1) 6 (20.7)	 51 (42.9) 23 (79.3)	 < 0.00
Type of Infection Tinea Corporis Tinea Cruris Both (Corporis & Cruris)	 58 (39.2) 33 (22.3) 57 (38.5)	 37 (63.8) 16 (48.5) 21 (36.9)	 21 (36.2) 17 (51.5) 36 (63.1)	 0.01

Table 2 shows the response assessment of both groups of patients to the treatment modalities biweekly for two months and also shows the relapse rate after one and two months after cessation of treatment.

Table 2. Response of both groups

Visits			Groups		*P*-value* (between two groups)
			Group I (Itraconazole & Terbinafine) N (%)	**Group II** (Itraconazole alone) N (%)	
Response Assessment	2nd Visit (2 weeks)	Marked Clearance	54 (73)	17 (23)	< 0.00
		Incomplete Clearance	20 (27)	27 (36.5)	
		No Change	0	30 (40.5)	
	3rd Visit (4 weeks)	Complete Clearance	27 (36)	0	< 0.00
		Marked Clearance	47 (64)	29 (39)	
		Incomplete Clearance	0	45 (61)	
	4th visit (6 weeks)	Complete Clearance	44 (59)	18 (24)	< 0.00
		Marked Clearance	30 (41)	39 (53)	
		Incomplete Clearance	0	17 (23)	
	5th visit (8 weeks) End of treatment	Complete Clearance	68 (92)	35 (47)	< 0.00
		Marked Clearance	6 (8)	33 (45)	
		Incomplete Clearance	0	6 (8)	
Relapse Assessment	6th Visit (12 weeks)	Present	3 (4)	30 (40.5)	< 0.00
		Absent	71 (96)	44 (59.5)	
	7th Visit (16 weeks)	Present	5 (7)	42 (57)	< 0.00
		Absent	69 (93)	32 (43)	

***P- value based on Chi-Square**

At the second visit, after two weeks of treatment, marked clearance was achieved by 54 (73%) patients in group I and 17 (23%) patients in group II; incomplete clearance was achieved by 20 (27%) patients in group I and 27 (36.5%) patients in group II. All patients in group I showed either marked clearance or incomplete clearance, while 30 (40.5%) patients in group II still have no change (Figure 1). There was a significant difference in response to treatment between the two groups (p value < 0.00).

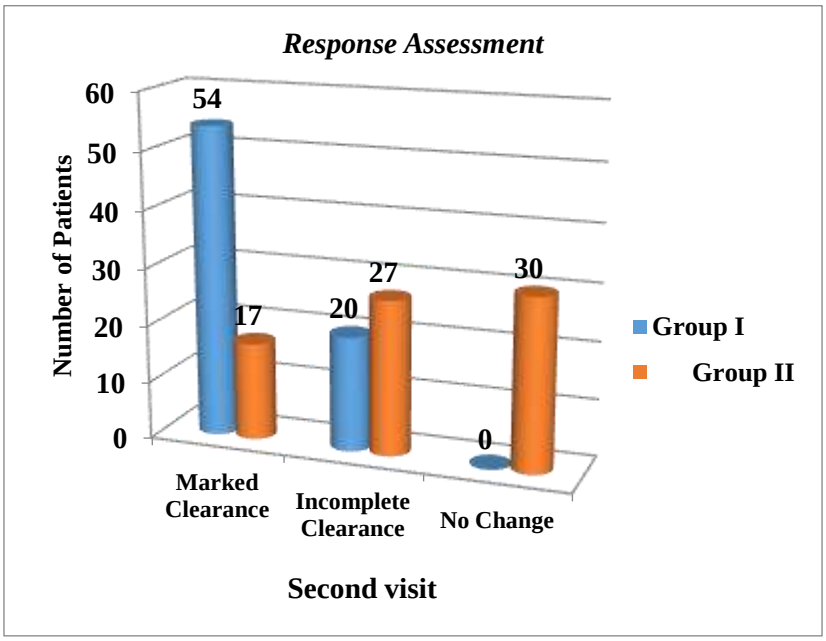

Figure 1. Response of both groups after two weeks

At the third visit, after one month of treatment, 27 (36%) of patients in group I achieved complete clearance of lesions, while nobody in group II achieved this complete clearance at that time of visit. Marked clearance was reported in 47 (64%) of patients in group I and 29 (39%) of patients in group II. There was a significant difference in response to treatment between the two groups (p value < 0.00). At this visit, all patients in group I showed either complete clearance or marked clearance; there was no incomplete clearance. Patients in group II, their response changed either to marked clearance or incomplete clearance. As a result, all patients in both groups showed a response to the treatment modalities (Figure 2).

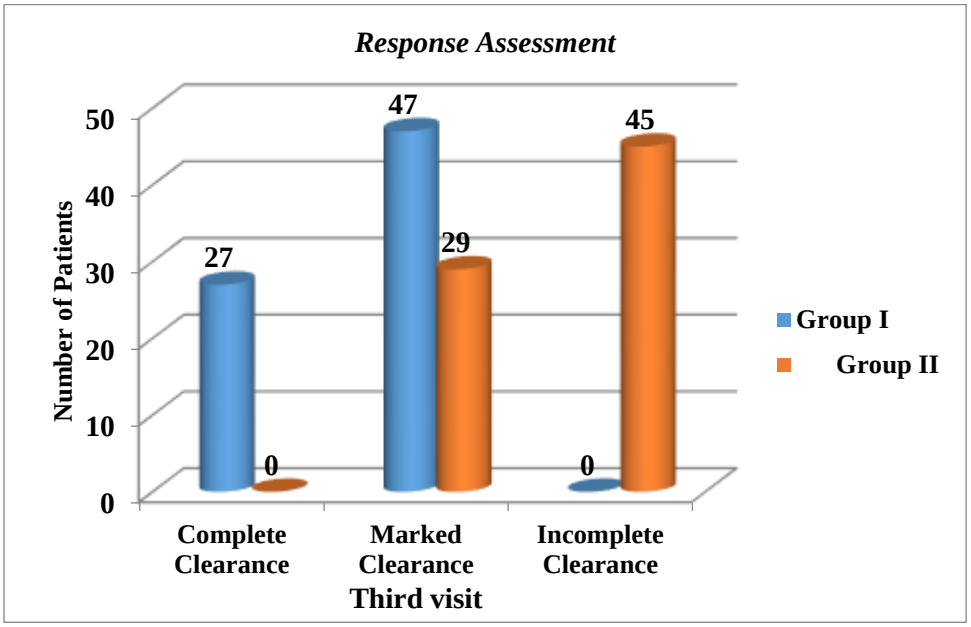

Figure 2. Response of both groups after four weeks

At the fourth visit, after 6 weeks, there was a significant difference (p value < 0.00) between the two groups, with a complete clearance achieved by 44 (59%) patients in group1 while only 18 (24%) in group II; marked clearance achieved by 30 (41%) in group I and 39 (53%) in group II. None of the patients in group I showed incomplete clearance, while 17 (23%) patients in group II still have incomplete clearance (Figure 3).

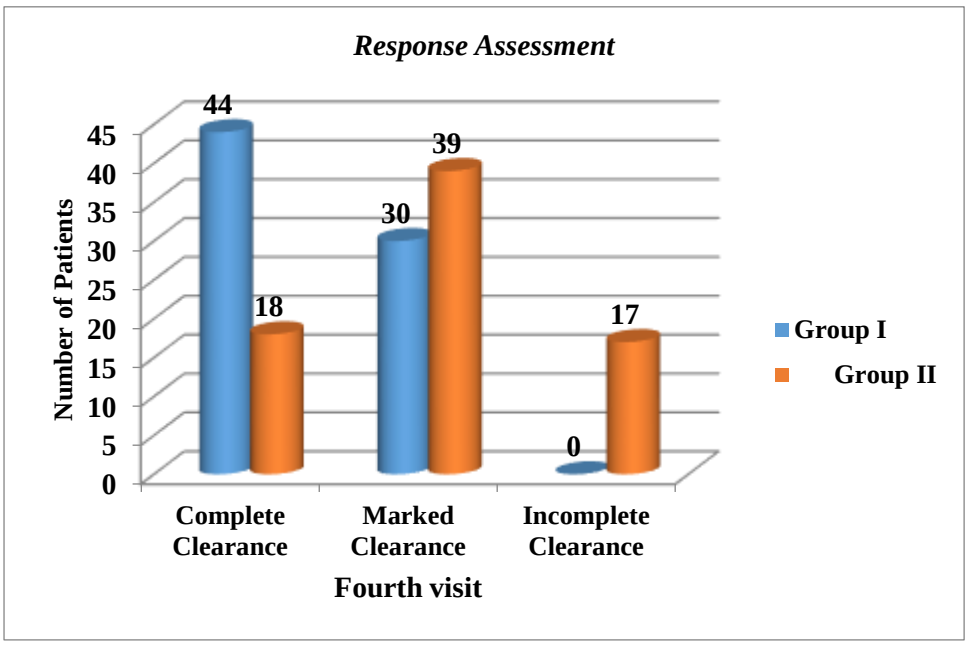

Figure 3. Response of both groups after six weeks

At the fifth visit, after 8 weeks, complete clearance was 68 (92%) in group I and 35 (47%) in group II; marked clearance was 6 (8%) in group I and 33 (45%) in group II. 6 (8%) patients in group II still have incomplete clearance. There was a significant difference between the two groups, p value < 0.00 (Figure 4).

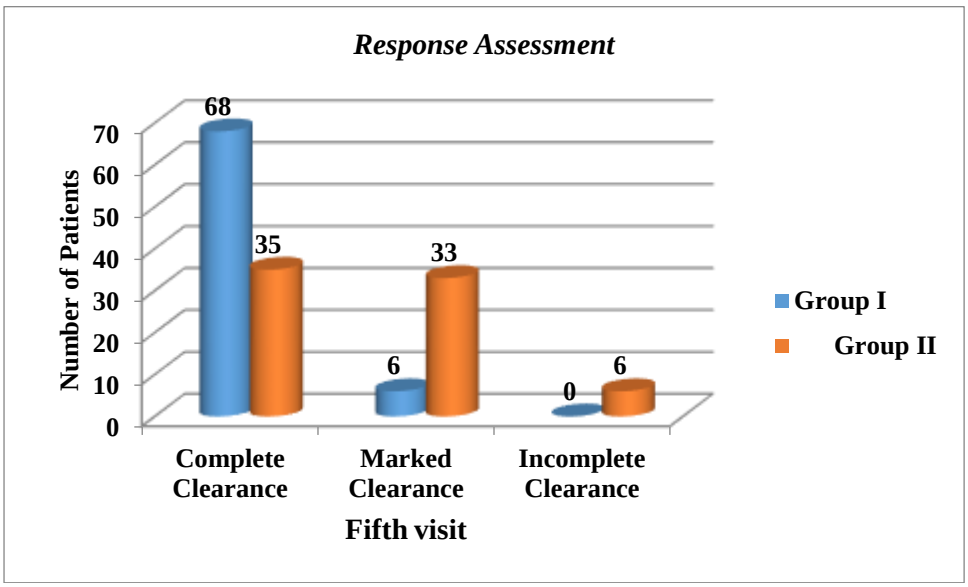

Figure 4. Response of both groups after eight weeks.

In the assessment of response to the treatment in follow-up visits, patients in group I who achieved complete clearance were 0, 27, 44, and 68 in the second, third, fourth, and fifth visits respectively versus 0, 0, 18, and 35 respectively in group II (Figure 5).

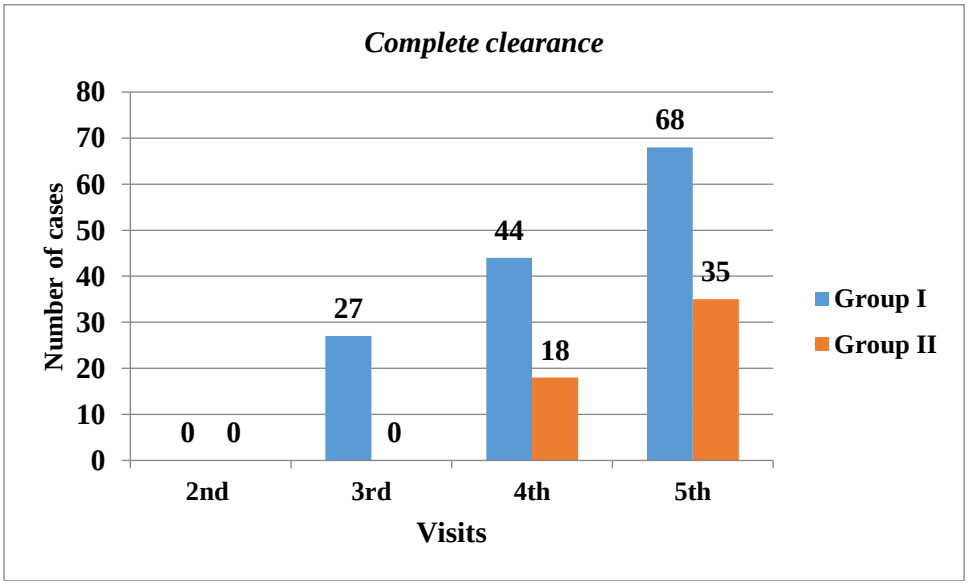

Figure 5. Complete clearance of both groups in the follow-up visits.

In the assessment of relapse, after one month of completion of treatment (sixth visit), only 3 (4%) patients relapsed in group I, while 30 (40.5%) relapsed in group II, and the difference was highly significant (p value < 0.00) between the two groups (Figure 6).

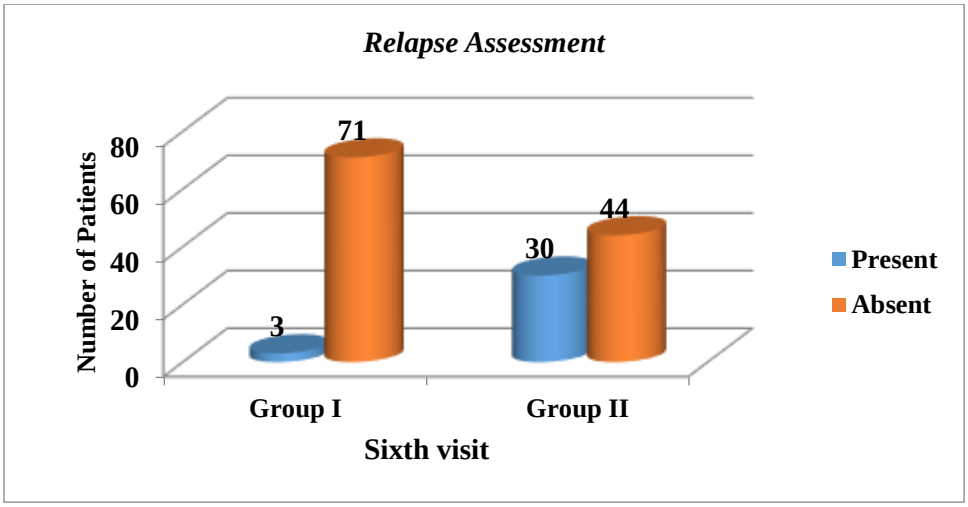

Figure 6. Relapse of both groups after twelve weeks.

At the seventh visit, after 16 weeks, 5 (7%) relapses were in group I, while 42 (57%) relapses were in group II, and there was a significant statistical difference between both groups p value < 0.00 (Figure 7).

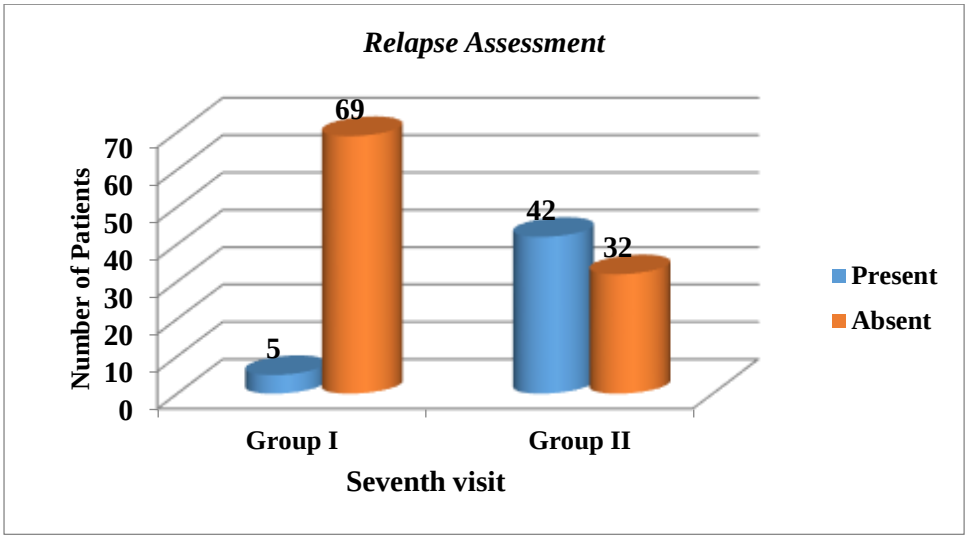

Figure 7. Relapse of both groups after sixteen weeks

The relapse rate of total patients was higher in males 38/98 (38.77%) than females 9/50 (18%) (Table 3), and it was lower in patients with positive family history 32/119 (26.89%) than the patients with negative family history 15/29 (51.72%) (Table 4).

Table 3. Relapse in both sexes

Sex	**16th week follow-up for relapse**		***P*-value**
	Present	**Absent**	
Male	38	60	0.01
Female	9	41	

Table 4. Relapse in patients with family history of tinea

Family history of infection	**16th week follow-up for relapse**		***P*-value**
	Present	**Absent**	
Positive	32	87	0.01
Negative	15	14	

The reported adverse effects were mild and transient like nausea, diarrhea, constipation, abdominal discomfort, and headache. None of the patients reported higher than two times serious or toxic rise in liver enzymes.

Discussion

Recently, across the world, there has been an increasing prevalence of dermatophytosis, especially in the tropics. Iraq is one of the many countries that is facing a wide spread of chronic, relapsing, and resistant dermatophytosis in a way that has never been encountered before [8]. It is important for the dermatologist to look beyond the likelihood of resistant tinea. The particular mechanisms behind the emergence of chronic dermatophytosis are still unclear. There is a strong need for alternative treatment options. Corporations with other correlated pharmacological specialties are necessary, including this study regarding the kind, dose, and the course of oral antifungal treatment.

Many earlier studies showed that the prevalence of dermatophytosis is higher in males than females [31-35], and some Iraqi researchers also reported this finding [9-10, 12], and this was consistent with our present study that showed there was a statistically significant difference in the incidence of tinea infection between males and females; 98 (66.2%) were males and 50 (33.8%) were females. This disparity may be related to the increased exposure of males to outdoor activities, which increase their sweating, or may be related to the sanitary awareness of females toward the environment and hygiene. Campillo et al.[36] and Capek and Simek [37] reported that progesterone can inhibit the growth of *T. mentagrophytes*. However, some studies showed the incidence of dermatophytosis is higher in females than males [38-40].

The family history of dermatophytes infection in this study was positive in 80.4% of patients. High frequencies in close contact have been reported by recent studies [41-43] Verma and Madhu [44] explained that dermatophyte infections in multiple family members lead to increased infectivity of organisms due to the easily transferring of spores through linen, combs, fomites, and clothing. Sahoo and Mahajan [6] revealed that all family members are not equally susceptible to fungal infection under similar risk conditions. Jaradat et al. [45] reported that genetic predispositions such as beta-4 low defenses may lead to susceptibility to all dermatophytes.

The fungal cell membrane is the same biological target for the action of both itraconazole and terbinafine. Sterol 14-α-demethylase is inhibited by itraconazole, and squalene epoxidase is inhibited by terbinafine, both of which prevent the formation of ergosterol. Additionally, allylamines promote the buildup of lanosterol, a hazardous intermediate substance in the ergosterol production pathway [20-22].

Itraconazole is ideal for the treatment of cutaneous mycosis and has produced a consistently high cure rate [46]. Itraconazole is the most sensitive antifungal agent against different types of *Trichophyton* and *Microsporum nanum* [47]. Singh et al. [48] reported that itraconazole was the most effective and superior to fluconazole, griseofulvin, and terbinafine in comparison to these three drugs in the treatment of dermatophytosis. Karaca and Koc [49] reported that terbinafine was the most effective antifungal drug among itraconazole, ketoconazole, fluconazole, and other antifungal drugs against dermatophyte species. Terbinafine showed the highest anti-dermatophytic activity against different types of *Trichophyton*, *Microsporum*, and *Epidermophyton floccosum* [50]. Some studies reported that the cure rate for terbinafine was between 74% and 80% [51-52].

Terbinafine and itraconazole are common treatments for the dermatophyte tinea corporis [53]. A combination of different antifungal drugs has been achieved in an attempt to overcome the drug resistance of filamentous fungi or yeast [54-55]. Itraconazole and terbinafine have been used in combination for the management of dermatophytosis [23]. Because of the increasing appearance of chronic, resistant, and relapsing tinea corporis and/or tinea cruris in Iraq, in this study, we tried to assess the response of tinea infection to the combination therapy of itraconazole and terbinafine as they may provide synergistic effects by their different mechanisms of action [56-58].

After 2 weeks of treatment, marked clearance was achieved by 54 (73%) of patients in group I (combination therapy) while only 17 (23%) were achieved by patients in group II (itraconazole alone), and it was to be highly significant (p value < 0.00). After one month, 27 (36%) of patients showed complete clearance in group I, while no one in group II; however, at the end of the treatment duration (2 months), complete clearance in group I was 68 (92%), while in group II was 35 (47%). Statistically, there was a significant difference (p value < 0.00). In this study, the cure rate (complete and marked clearance) was (100%) in group I. This was consistent with a study by Sharquie and Jabbar [8], in which ketoconazole and terbinafine was used. These results were much higher than in other studies in which terbinafine and itraconazole were used alone [23-25]. Sharma et al. [23] reported that the cure rate was 90% in a study where a combination of terbinafine and itraconazole was used.

The observed relapse rate, after 2 months of discontinuation of treatment, was 5 (7%) in group I and 42 (57%) in group II and it was highly significant (p value < 0.00). This explains why the relapse rate with monotherapy for tinea infections is higher than with combination treatment. Khurana et

al. [59] reported that the relapse rate in totally cured patients on itraconazole 200 mg/day was 41.5%. The relapse rate after two weeks on terbinafine 250 mg/day was 57% [23]. The relapse rate was higher in males 38/98 (38.77%) than females 9/50 (18%) and it was statistically significant (p value 0.01). Higher relapses in males than females may be attributed to their outdoor activities, which increase their sweating, or may be attributed to their poor compliance with the hygiene practices. The relapse rate was highly significant (p value 0.01) in patients with negative family history, 15/29 (51.72%) compared to those with positive family history, 32/119 (26.89%). This finding was not consistent with the result of Khurana et al study where the occurrence of relapse had no statistically significant association with family history of tinea [59].

Safety was assessed by noticing any serious or adverse effects. Almost all the noted drawbacks in both groups were mild and didn't warrant discontinuation of treatment. Earlier studies reported that these drugs, either in combination or as monotherapy, were safe [10, 23, 60]. Itraconazole and terbinafine rarely cause liver injury, although they have a tendency to cause hepatotoxicity [61]. Liver function tests were investigated in all patients, and none of the patients showed a serious or toxic rise in the liver enzymes.

Conclusion

Combination of itraconazole and terbinafine induced early significant complete and marked clearance. They are approved to be better than itraconazole monotherapy as they provide a synergistic activity and can be used as an alternative for patients with chronic tinea corporis and/or tinea cruris. They were safe, well tolerated and decreased relapse rate.

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Conflicts of Interest

The authors declare no conflicts of interest.

Funding

The authors did not receive any funds.

Ethics Statements

This study obtained an approval and permission from the Anbar Health Directorate, Center of Training and Human Development, Research Committee (Ref. No. 2022041 dated 29/5/2022).

Author Contribution

Examination of patients and inclusion them in the study: Thamir; Data gathering: Thamir & Yagub; practical (follow up the patients), analysis of data, and written parts of the study: Yagub; final approval and agreement for all aspects of the study, supervision, revision and rearrangement: Thamir and Basim.

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إيتراكونازول وتيربينافين مقابل إيتراكونازول كنظام جديد لعلاج السعفة المزمنة الناشئة حديثاً: دراسة سريرية مقارنة.

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الخلاصة

الفطار الجلدي هومن أكثر الأمراض الفطرية المعدية شيوعًا. ويواجه العراق، مثل العديد من البلدان الأخرى حول العالم، ظهور حالات الاصابة بالسعفة المزمنة والمقاومة للعلاج والانتكاسية. قارنت هذه الدراسة فعالية وسلامة ومعدل الانتكاس لنظام علاجي مركب من إيتراكونازول وتيربينافين مقابل إيتراكونازول فقط في علاج عدوى السعفة المزمنة. تم تقسيم المرضى بالتساوي إلى مجموعتين حيث تلقت المجموعة الأولى مزيجًا من إيتراكونازول وتيربينافين بينما تلقت المجموعة الثانية إيتراكونازول فقط لمدة ثمانية أسابيع لكل مجموعة.اما لتقييم معدل الانتكاس، فقد كانت المتابعة لمدة شهرين. لقد كان هناك ١٤٨ فقط من أصل ١٦٠ من المرضى المسجلين الذين أكملوا الدراسة حيث ان ٩٨ (٦٦,٢٪) كانوا من الذكور و٥٠ (٣٣,٨٪) كانوا من الإناث. وكان متوسط العمر (±الانحراف المعياري) لجميع المرضى هو ٣٣,٠٤ ± ١٢,٦٥سنة. لم يكن هناك فرق كبير في محل سكناهم. وكان تاريخ العائلة من حيث الاصابة بالمرض إيجابيا في غالبية المرضى فقد تحقق في ١١٩ (٨٠,٤٪) منهم. بعد أسبوعين من بدأ العلاج، كان هناك اختلاف كبير في الاستجابة للعلاج، حيث تم تحقيق تصفية ملحوظة لمنطقة الاصابة من قبل ٥٤ (٧٣٪) مريضا في المجموعة الأولى، و ١٧ (٢٣٪) مريضا فقط في المجموعة الثانية. وبعد ٨ أسابيع، كانت التصفية الكاملة ٦٨ (٩٢٪) في المجموعة الأولى، و ٣٥ (٤٧٪) في المجموعة الثانية، وكانت التصفية الملحوظة في ٦ (٨٪) في المجموعة الأولى، في حين ٣٣ (٤٥٪) في المجموعة الثانية. وكان ٦ (٨٪) من المرضى في المجموعة الثانية لا يزال لديهم تصفية غير كاملة. لقد كان معدل الانتكاس بعد ١٦ أسبوع هو ٥ (٧٪) في المجموعة الأولى، بينما كان ٤٢ (٥٧٪) في المجموعة الثانية. ولقد خلصنا في هذه الدراسة إلى أن النظام العلاجي للإيتراكونازول والتيربينافين كان فعالاً وآمنًا وجيد التحمل مع انخفاض في معدل الانتكاس.

الكلمات المفتاحية: مضاد للفطريات، فطار جلدي مزمن، إيتراكونازول، تيربينافين.