

## Recent Modality in the Treatment of Recalcitrant Dermatophytosis

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### *Abstract*

**Background:** *Dermatophytosis is a common skin disease in Egypt. It is caused by keratinophilic fungi. Tinea become chronic, recurrent and resistant to traditional therapies. Isotretinoin is a good adjuvant to systemic antifungal in chronic dermatophytosis due to its keratolytic effect.*

**Aim:** *This is a prospective study to assess the effectiveness of combined oral itraconazole/isotretinoin therapy in the treatment of chronic and recalcitrant dermatophytosis.*

**Patients and Methods:** *A total of 30 patients with chronic and/or recalcitrant dermatophytosis were included. Potassium hydroxide microscopy was performed. All the patients received combined oral itraconazole/isotretinoin therapy; Itraconazole 200 mg twice daily with adjuvant isotretinoin 20 mg daily for 6 weeks. The patients were followed up to 6 months for signs of recurrence.*

**Results:** *Mycological cure was observed in 83.3% and complete cure occurred in 70% of the patients.*

**Conclusions:** *Combined oral itraconazole/isotretinoin therapy could be an effective treatment in recalcitrant dermatophytosis.*

**Keywords:** *Itraconazole; isotretinoin; recalcitrant; dermatophytosis`*

### **Introduction**

Dermatophytes are keratinophilic fungi responsible for skin, nail, and scalp infections, which compose the most common types of superficial cutaneous fungal infections seen in humans and animals. There is recent increase in the number of patients with dermatophytosis and the chronicity of this superficial infection has been observed. Chronic dermatophytosis, defined as a persistent infection for six months or longer.<sup>(1, 2)</sup>

The various factors attributable to this trend are environmental factors, erratic use of antifungal agents, irrational use of topical steroids combinations, an increasing resistance to antifungal agents, genetic susceptibility and socio-economic status.<sup>(3)</sup>

A potassium hydroxide (KOH) preparation is used to confirm the diagnosis. The treatment is challenging because of recurrences and/or resistance. Topical treatment has a limited role. Systemic antifungal drugs like Griseofulvin, ketoconazole and terbinafine do not achieve complete cure.<sup>(4)</sup>

Itraconazole is a triazole antimycotic agent with strong keratophilic and lipophilic properties that involves inhibition of 14- $\alpha$ -demethylase, resulting in impaired sterol synthesis in fungal cell membrane. It is also increasingly being used as a first-line drug for tinea corporis and tinea cruris, but it is being given for longer periods and still there are relapses with itraconazole treatment. So, an effective adjuvant is needed to reduce the time duration of oral antifungals and recurrence rate. Isotretinoin was found to be good adjuvant treatment in recalcitrant dermatophytosis due to its keratolytic and immunomodulatory effect.<sup>(5,6)</sup>

So, we performed a clinical trial to assess the effectiveness of combined oral itraconazole/isotretinoin therapy in the treatment of recurrent and recalcitrant dermatophytosis.

### **Patients and Methods**

**Patients:** Thirty patients with chronic and/or recalcitrant dermatophytosis were included in the study after approval by the institutional review board (IRB) of Medical School at Zagazig University, Egypt. Informed consent was obtained from each patient and extremely detailed information about nature of the study was explained. Patients with hyperlipidemia, liver or kidney function impairment, pregnant and lactating females were excluded from the study.

### **Methods:**

Thirty patients received a combined therapy of oral itraconazole 200 mg/day plus oral isotretinoin 20 mg/day. Treatment was administered for 6 weeks.

Response to treatment was evaluated by the decrease in inflammation and scaling, decreased itching and photographic comparison at each visit, along with mycological assessment by direct KOH microscopy (**Figure 1**).

Adverse effects were also evaluated and laboratory investigations included complete blood picture, liver and kidney function tests, and lipid profile.

Treatment efficacy was defined by complete cure that includes both clinical cure (clinically completely normal skin) and mycological cure (negative KOH microscopy).

### Follow up

Follow up of patients was done every month for 6 months for detection of any recurrence of dermatophytosis.

### Results

All patients completed the study and the follow-up period. The age of patients ranged from 9 to 59 years. Male patients were predominant, lived in rural areas and risk factors included immunosuppressive state, animal contact, other family members affected, history of topical steroids and travel to endemic areas (Table 1).

#### Therapeutic response:

Mycological cure occurred in 83.3% of patients. Clinical cure occurred in 70% of patients. Complete cure, which involves both mycological and clinical cure, was noted in 70% (Table 2 & figure 2).

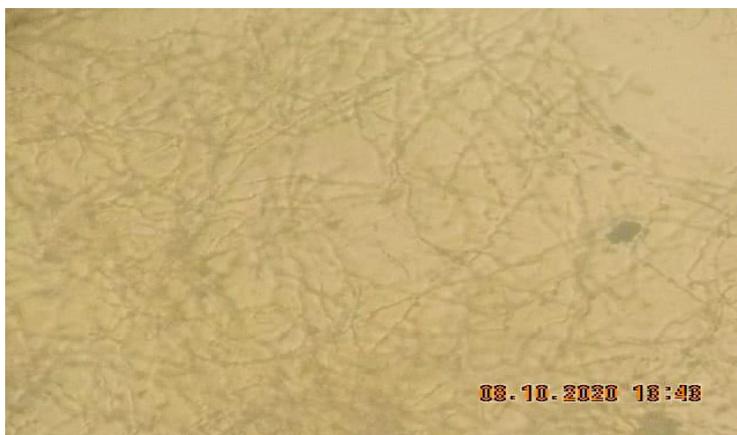
#### Adverse effects:

Adverse effects were mild and well tolerated in the form of cheilitis and xerosis that were noted in most patients.

#### Recurrence

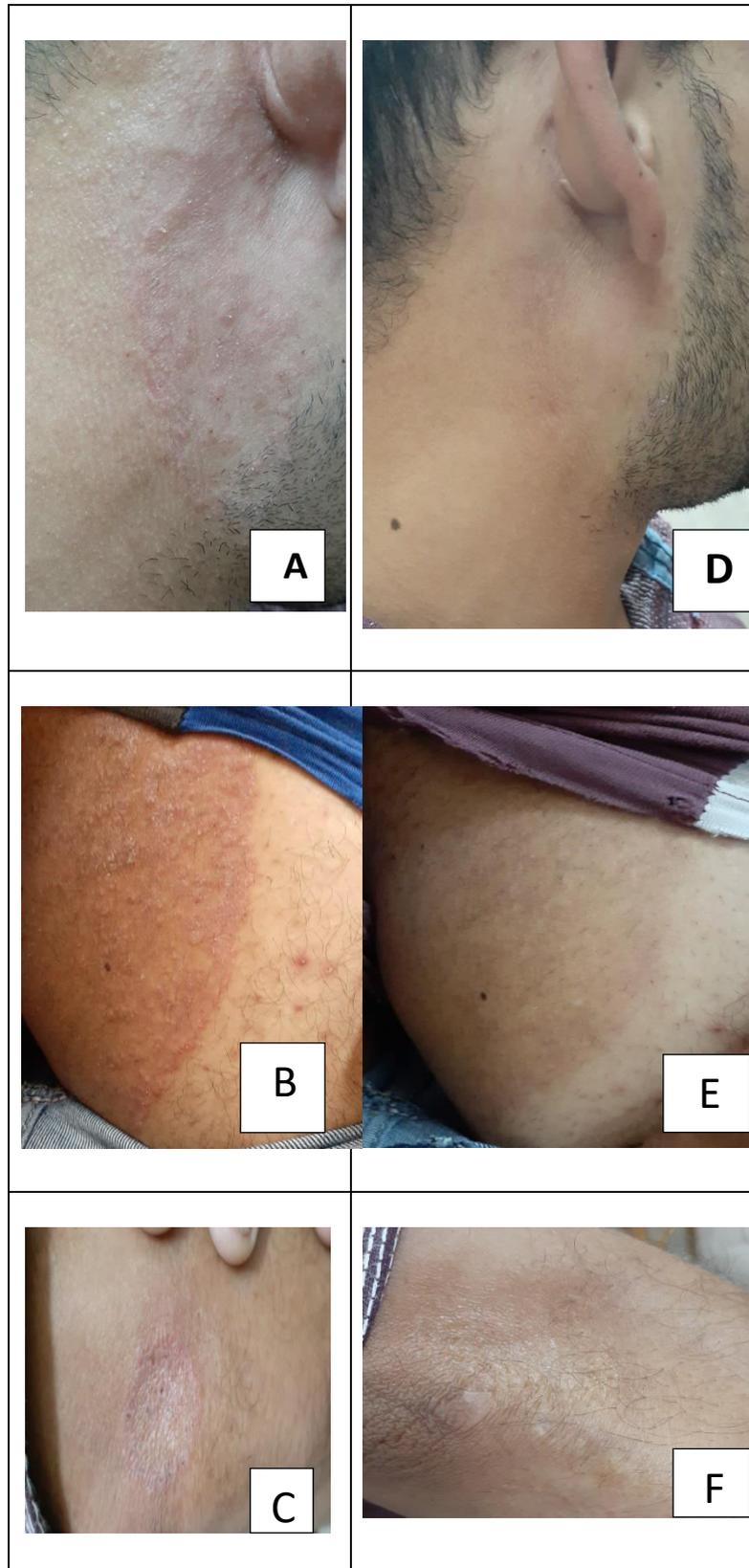
Recurrence occurred in 7 from the 25 mycologically-cured patients (Recurrence rate: 28%)

#### Figure 1: Direct potassium hydroxide (KOH) microscopy of the skin lesion scraping.



**Figure (1):** Direct potassium hydroxide (KOH) microscopy of the skin lesion scraping showing hyaline Septate hyphae (Original magnification X 400)

**.Figure 2: Combined oral itraconazole/isotretinoin therapy for recalcitrant dermatophytosis.**



**Figure (2): (A,B&C) Multiple site tinea in in a 25-year-old male patient ; in the neck, crural area and elbow before treatment of combined itraconazole and isotretinoin**

(D,E&F) Complete cure at the end of 6 week-combined itraconazole and isotretinoin therapy.

**Table (1):** Basic characteristics of the studied groups:

	N=30	
	N	%
<b>Age</b>	<b>36.1 ± 15.3</b>	
<b>Median</b>	<b>30</b>	
<b>Range</b>	<b>9 - 59</b>	
<b>Sex</b>		
Male	<b>21</b>	<b>70</b>
Female	<b>9</b>	<b>30</b>
<b>Residence</b>		
Urban	<b>13</b>	<b>43.4</b>
Rural	<b>17</b>	<b>56.6</b>
<b>Occupation</b>		
Housewife	<b>7</b>	<b>23.3</b>
Farmer	<b>4</b>	<b>13.3</b>
workers	<b>9</b>	<b>30</b>
Non related jobs (accountant,teacher, lawyer, student...)	<b>10</b>	<b>33.3</b>
<b>+ve family history</b>	<b>21</b>	<b>70</b>
<b>Complaint</b>		
Disfigurement	<b>10</b>	<b>33.3</b>
Itching	<b>30</b>	<b>100</b>
<b>Risk factors</b>		
Immunosuppressive state	<b>6</b>	<b>20</b>
Animal contact	<b>5</b>	<b>16.7</b>
Other family members affected	<b>21</b>	<b>70</b>
History of topical steroids	<b>13</b>	<b>43.3</b>
Travel to endemic area	<b>8</b>	<b>26.7</b>

**Table (2):** Therapeutic response after completion of therapy.

	N=30	
	N	%
<b>Mycological cure</b>		
Positive	<b>5</b>	<b>16.7</b>

Negative	25	83.3
<b>Clinical cure</b>		
Complete	21	70
Incomplete	9	30

## Discussion

There is an increase in cases of recalcitrant, recurrent, chronic and atypical dermatophytosis. Many antifungals are being used for complete cure, but success often are not being occurred.<sup>(7)</sup>

Isotretinoin was found to be good adjuvant therapy to increase cure rates and decrease recurrence rate of emerging atypical, chronic, recurrent and recalcitrant dermatophytosis. The proposed mechanisms of therapeutic success with isotretinoin, when added to itraconazole are increased epidermal cell turnover thereby eliminating the growing dermatophyte, increase in skin pH that inhibits dermatophyte growth, and immunomodulatory effect.<sup>(6)</sup>

The results of the present study revealed that mycological cure was noted in 83.3% and complete cure was observed in 70% of the studied patients. This cure rate was much lower than that reported by **Rahman(2019)**<sup>(8)</sup> that showed higher cure rates with mycological cure in 95% and complete cure in 90% of patients. This difference may be attributed to the longer duration of the therapy of 3 months in his patients versus the shorter duration of 2 months only in our study.

Moreover, successful treatment of a patient suffering from recurrent cutaneous dermatophytosis with systemic isotretinoin and itraconazole was previously reported by **Ardeshna et al. (2016)**.<sup>(6)</sup> Oral isotretinoin (20 mg/day) and itraconazole (200 mg/day) were given for a period of 1 month. His patient showed complete response and no recurrence occurred after follow up for 6 months.

Recurrence was observed in 7 out of 25 mycologically-cured patients (28%). This recurrence rate is higher than that reported by **Rahman(2019)**(15%).<sup>(8)</sup>

## Conclusion

In conclusion, Isotretinoin seems to be a good adjuvant to systemic antifungals in the treatment of chronic and recalcitrant dermatophytosis.

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