



## Original Article

# Study on Efficacy and Safety of Terbinafine Vs. Itraconazole in the Treatment of Tinea Pedis

Lt Col Md Humayun Kabir,<sup>1</sup> Brig Gen (Rtd) Md Abdul Latif Khan,<sup>2</sup> Col Md Shirajul Islam Khan,<sup>3</sup>  
Lt Col A T M Rezaul Karim,<sup>4</sup> Md. Mostafizur Rahman,<sup>5</sup> Ahmed Masiha Jamil<sup>6</sup>

### Abstract

**Background:** Tinea pedis is a dermatophytosis of the feet usually occurs between the toes with the webspace between the fourth and fifth digits but, in many cases, may appear as an extensive pattern on the bottom and sides of the feet. Terbinafine and itraconazole were evaluated with the efficacy/effectiveness and toxicity in the systemic treatment of Tinea pedis and compared with each other.

**Objective:** To compare the efficacy and safety of terbinafine vs. itraconazole in treating tinea pedis.

**Materials and Methods:** A total of 50 patients were selected, and they were divided into groups (group-A and group B), each of which included 25 patients. Group A was given oral Terbinafine 250 mg daily for two weeks. Group B was given oral Itraconazole 200mg daily for the same duration. Patients were observed for the efficacy and side effects of the trial medicines. A baseline complete blood picture, liver and renal function test, and urine analysis were done and repeated frequently during therapy.

**Results:** Most patients were in the fourth decade in both groups, and the male-to-female ratio was almost 4:1. Two groups of people were studied: group-A with terbinafine 250 mg daily and group B with itraconazole 200 mg daily for 14 days. Evaluated weekly during treatment and 02 weeks after cessation of therapy, and finally on 08<sup>th</sup> week to see the clinical improvement and adverse effects. The clinical response was found in chronic hyperkeratotic type: 08/08, 08/08; chronic interdigital type: 07/07, 07/06; vesico-bullous type: 06/05, 06/05; Mixed type: 04/03, 03/02 in group-A and group-B respectively. On average, 92% clinical improvement was found in group-A and 84% in group B. Most patients had nausea (20.0%) followed by 08% diarrhea in group A. On the other hand, in group B, most patients had nausea (28.0%), followed by 4.0% fatigue and 4.0% diarrhea, and only 01 patient had elevated liver enzyme but did not exceed the upper limit. 80% of patients in the terbinafine group had transient, mild to moderate nausea.

**Conclusion:** No significant differences in efficacy and toxicity were found between terbinafine and itraconazole groups. Terbinafine may represent a good alternative for treating Tinea Pedis in patients who cannot take itraconazole or other available drugs due to contraindications.

**Key-words:** Complete blood count (CBC), liver function test (LFT)

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### Introduction

Tinea pedis, also known as athlete's foot is a dermatophytosis of the feet and is by far the most common fungal disease caused by predominantly *Trichophyton rubrum*, *Trichophyton*

*mentagrophytes* and *Epidermophyton floccosum*.<sup>1</sup> It usually occurs between the toes, with the webspace between the fourth and fifth digits, but in many cases may appear as an extensive "moccasin" pattern on the bottom and sides of the

<sup>1</sup> Classified Dermatologist, Combined Military Hospital (CMH), Dhaka.

<sup>2</sup> Professor and Ex-Adviser Specialist in Dermatology, CMH, Dhaka.

<sup>3</sup> Professor & Head, Department of Dermatology & Venereology, CMH Dhaka.

<sup>4</sup> Associate Professor & Head, Department of Dermatology & Venereology. Armed Forces Medical College, Dhaka.

<sup>5</sup> Assistant Professor, Department of Dermatology, Rajshahi Medical College, Rajshahi, Bangladesh.

<sup>6</sup> Assistant Professor, Department of Medicine. Rajshahi Medical College, Rajshahi, Bangladesh.

feet.<sup>2,3</sup> Tinea pedis most often is related to footwear. More occlusive shoes are associated with higher chances of tinea pedis. The infection is more common in summer months and in tropical climates.<sup>3</sup>

There are several distinct forms of tinea pedis encountered in clinical practice.

- a. Chronic hyperkeratotic type (moccasin).
- b. Chronic Interdigital type.
- c. Vesico-bullous type.
- d. Mixed type.
- e. Acute ulcerative.

Diagnosis of tinea pedis is based on the history and clinical appearance of the feet in addition to direct microscopy of a potassium hydroxide (KOH) preparation and Cultures; histological examinations are rarely required.<sup>2</sup>

Terbinafine is a synthetic antimycotic agent, one of the first antifungals of the allylamine class. Terbinafine is an antifungal effective against Dermatophytes, *Aspergillus* sp. and *Candida*, and *Pityrosporum* yeasts. Terbinafine has both fungistatic and fungicidal effects on dermatophytes. The advent of terbinafine has revolutionized the therapy of tinea pedis because this drug has high clinical and mycological cure rates.<sup>8</sup>

Itraconazole is a triazole that was synthesized in 1980. Itraconazole was approved in the USA for treating systemic mycoses in Sept 1992. It is a fungistatic drug like other azoles. It is highly lipophilic and is extensively metabolized in the liver. Itraconazole is also effective against dermatophytes and deep fungal infections. It is available in systemic and topical formulations.

On the institutional and personal level, many studies were performed in different parts of the world on treating tinea pedis. More local data is needed to assess the comparative efficacy and safety trial on tinea pedis with terbinafine and itraconazole. So, to treat the patient of tinea pedis in an effective way, such kind of study is necessary for our country on this common problem.

## Materials and Methods

This cross-sectional study was conducted in the Department of Dermatology & Venereology, Combined Military Hospital (CMH) Dhaka, from Jan 2013 to July 2013. Fifty patients with confirmed cases of Tinea pedis (Clinical and/or direct microscopy of a potassium hydroxide (KOH) preparation and Cultures) attending the department were selected as samples of the study. Pregnant and lactating women, patients with other diseases like onychomycosis, nail psoriasis, lichen planus, contact dermatitis, congenital nail dystrophy, malnutrition, iron deficiency anemia, concomitant therapy with drugs having a possible interaction with terbinafine and itraconazole, patients with hepatic dysfunction were excluded from this study.

A total of 50 were primarily selected, and they were randomized using computer-generated code into two groups (group-A and group B), each of which included 25 patients. Complete history, general, physical, and dermatological examinations, and necessary laboratory investigations were made for all enrolled patients. For women of reproductive age, reproductive history, menstrual history, lactation, and pregnancy were carefully judged. History and physical findings were recorded in a structured questionnaire. Finally, those patients, who matched the inclusion and exclusion criteria according to history, and physical examination and freely gave their informed consent were selected for the study. The diagnosis was made on a clinical basis, fungal microscopy, and culture. After confirming the diagnosis, Group A was given oral Terbinafine 250 mg daily for 02 weeks. Group B was given oral Itraconazole 200mg daily for the same duration. Patients were observed for the efficacy and side effects of the trial medicines. A baseline CBC, liver and renal function test, and urine analysis were done and repeated frequently during the course of therapy.

Patients were followed up on the 2nd, 4th, and finally, the eighth week to see clinical improvement and adverse effects. On each observation day, clinical symptoms

(dermatological findings) such as scales, keratinization, pruritus, redness, fissure, and vesicles, were observed, and improvement in clinical symptoms was classified into the following four stages:

1. Marked improvement: (over 75% improvement).
2. Significant improvement: (over 50%, <75% improvement).

3. Moderate improvement: (<50% improvement)

4. No change or mild improvement: (0%-improvement).

On each follow-up day, skin scrapings for fungal microscopy (by KOH preparation) and culture were done to see the presence or absence of fungal elements.

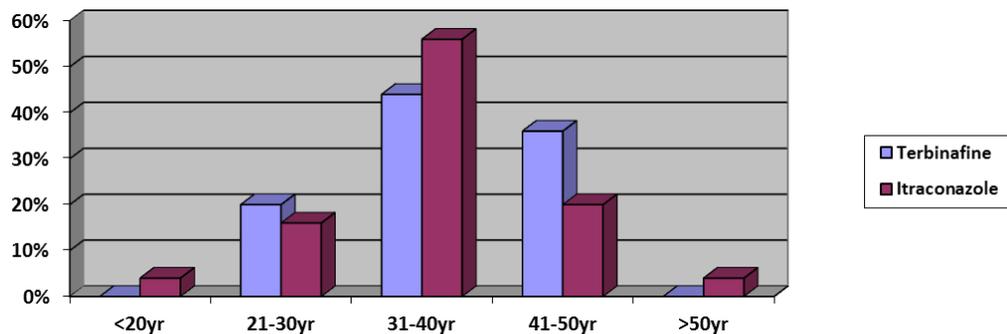
## Results

Data analysis was performed by Statistical Package for Social Science (SPSS), version-12. Data were edited, coded, and entered into the computer. The level of significance (p-value) was set at 0.05, and the confidence interval at 95%. Results were presented as text and tables.

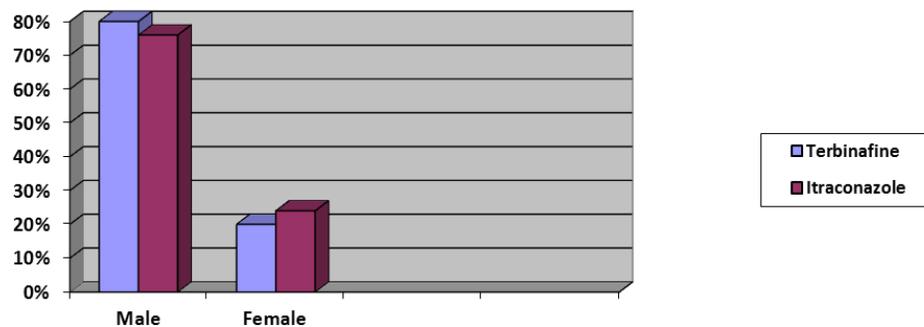
Group A: Patients treated with terbinafine

Group B: Patients treated with itraconazole

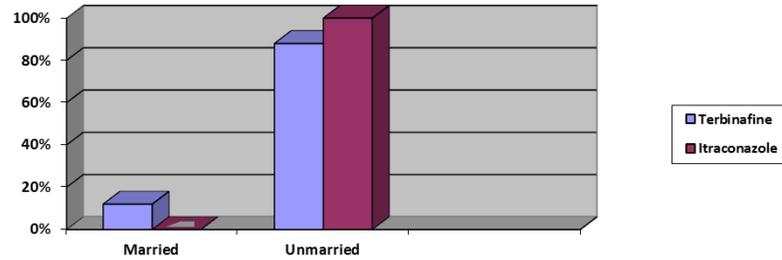
A total of 50 patients were included in this study; it was observed that the majority of patients were age belonged to 31-40 years in both groups.



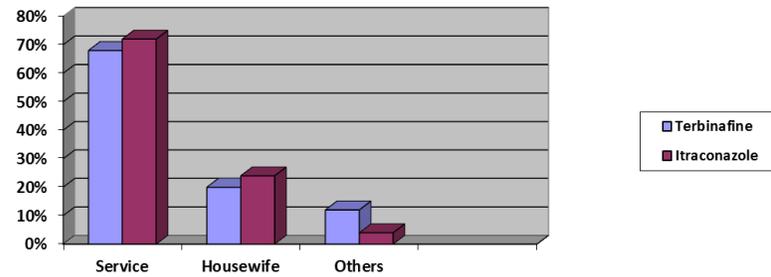
**Figure I: Bar diagram showing the age distribution of the study patients**



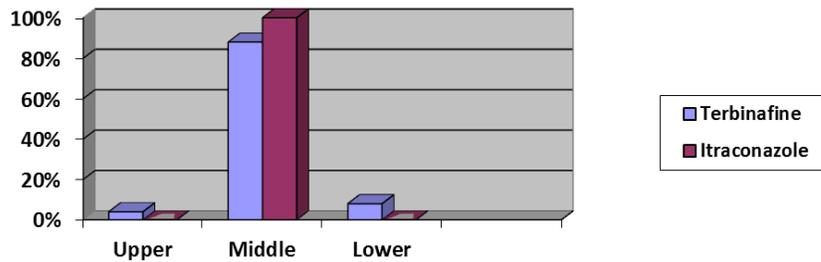
**Figure II: Bar diagram showing the sex distribution of the study patients**



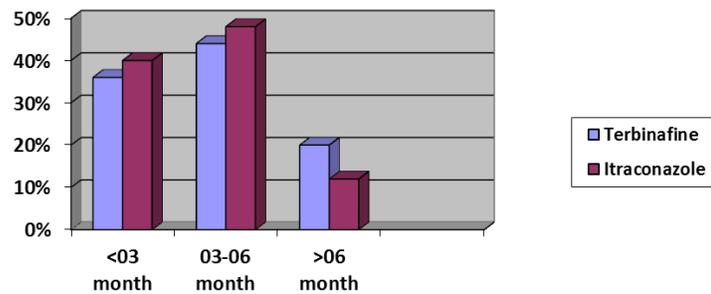
**Figure III:** Bar diagram showing the distribution of the patients by marital status



**Figure IV:** Bar diagram showing the distribution of the patients by occupational status



**Figure V:** Bar diagram showing the distribution of the patients by economic status



**Figure VI:** Bar diagram showing the distribution of the patients by duration of disease

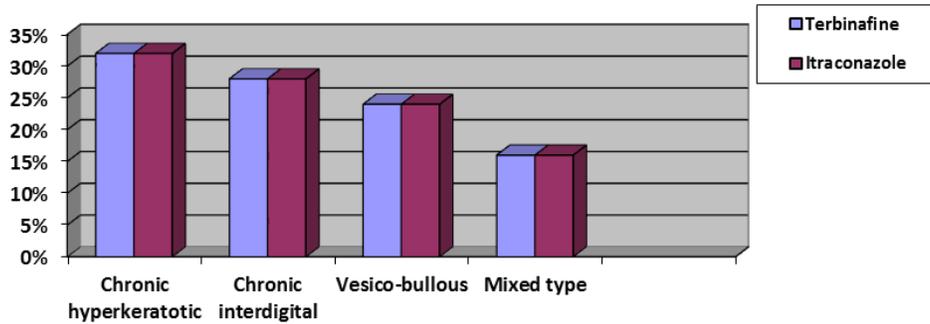


Figure VII: Bar diagram showing the clinical type of tinea pedis of the study patients

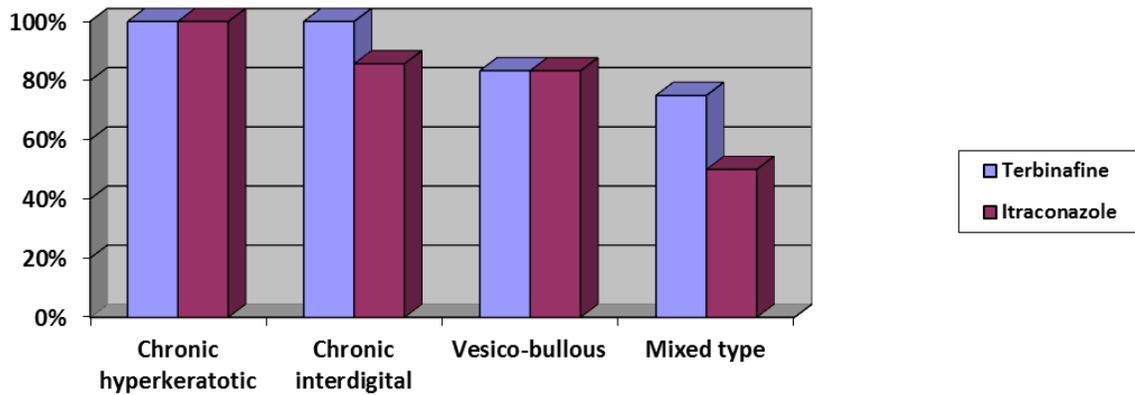


Figure VIII: Bar diagram showing Clinical response of tinea pedis of the study patients

Out of 25 patients in (**Group-A**) significant improvement was seen in 09 (36%) patients, moderate improvement was seen in 10 (40%) patients, and no change was observed in 06(24%) patients in <sup>the first</sup> week. However, in the second week, 12(48%) patients got marked improvement, and 03 (12%) had significant improvement; no changes or mild improvement was seen in 05(20%) patients, and in the 4th week, 19(76%) patients got marked improvement, whereas 03(12%) patients had moderate improvement and only 01 patient had no improvement.

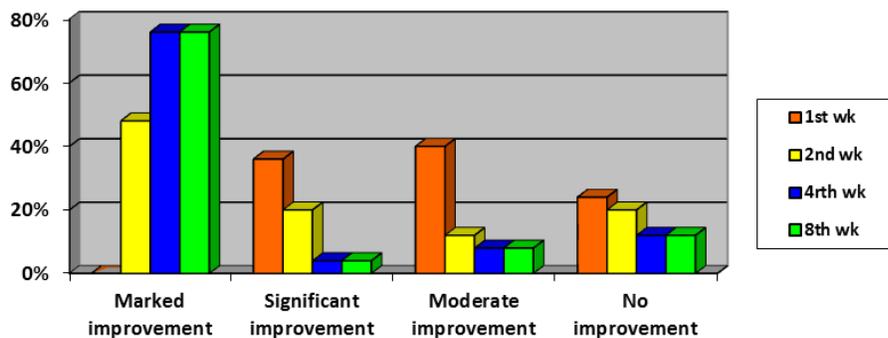
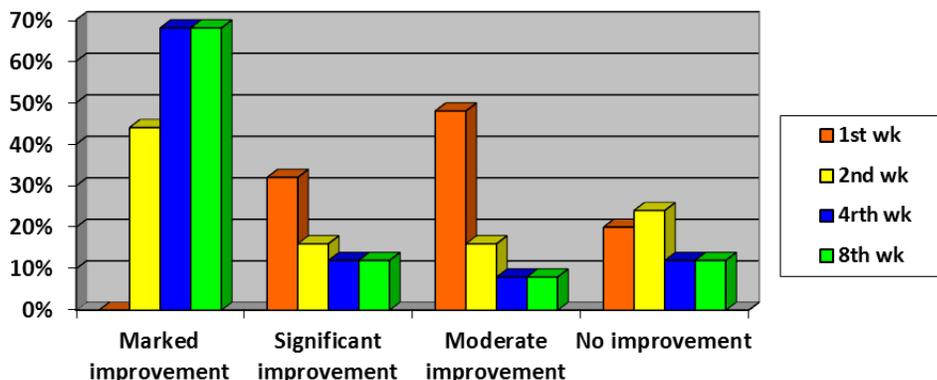
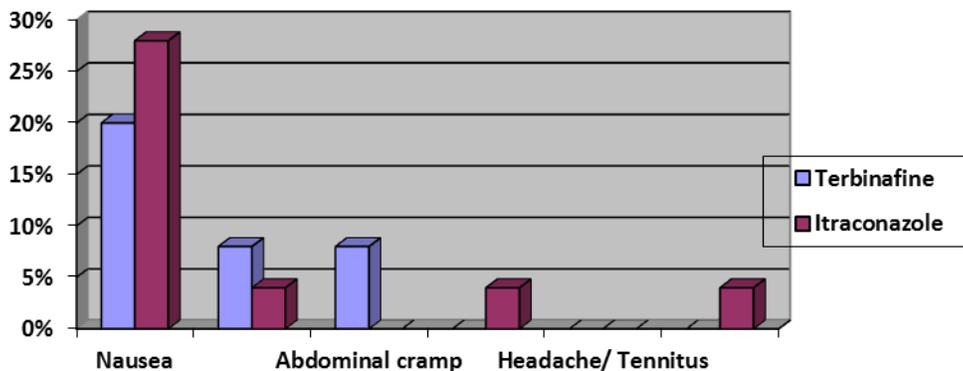


Figure IX: Distribution of treatment outcome (clinical improvement) of the patients by the first week, second week, fourth week, and eighth week.

Out of 25 patients in **(Group B)** significant improvement was seen in 08 (32%) patients, moderate improvement was seen in 12 (48%) patients, and no change was observed in 05(20%) patients in <sup>the first</sup> week. In the second week, 11(44%) patients got marked improvement, and 04 (16%) had significant improvement; no changes or mild improvement was seen in 06(24%) patients, and in the 4<sup>th</sup> week, 17(68%) patients got marked improvement, whereas 02(08%) patients had moderate improvement and only 03 patient had no improvement.



**Figure X: Distribution of treatment outcome (clinical improvement) of the patients by the first week, second week, fourth week, and eighth week.**



**Figure XI: Bar diagram showing the distribution of the patients by side effect**

**Discussion**

In this study, we have taken chronic hyperkeratotic, chronic interdigital type, vesicobullous type, and Mixed type of tinea pedis in both the group A and B. Group-A was given terbinafine 250 mg daily and itraconazole 200 mg daily in group B for two weeks to see the comparative efficacy and safety of terbinafine and itraconazole in the treatment of tinea pedis.

A total of 50 patients having tinea pedis patients attended the Department of Dermatology & Venereology, OPD, Combined Military Hospital

Dhaka Cantonment, from Jan 2013 to Jul 2013 were included in this study. Twenty-five patients were treated with terbinafine, and the rest 25 patients were treated with itraconazole, considered group A and group B respectively. Age below 18 years or above 60 years, pregnant and lactating mothers, patients taking other antifungal systemic drugs, patients suffering from liver and kidney diseases, and patients/attendants unwilling to give informed consent to participate in the study were excluded. The present study findings were discussed and compared with previously published relevant studies.

In the present study, a total of 50 patients were involved. Males 39 (78%) were more predominant in the study than females 11 (22%), which is consistent with other studies done by Lachapelle JM et al.<sup>17</sup> In this study, it was observed that tinea pedis was more common in male subjects, which was 80.0% in group A and 76.0% in group B. Dieridane A, Ammar-Khodja, et al.<sup>14</sup> showed that 40.0% and 55.6% were males in the terbinafine and itraconazole groups, respectively. In Bangladesh, less female predominance may be because female patients report less frequently because of a lack of health consciousness and religious bindings.

The majority of patients belonged between 31-40 years of age in both groups, which differs from other studies done by Wishart J.M.<sup>18</sup> In this current series, it was observed that married patients were predominant in both groups, which were 88.0% and 100.0% in group A and group B respectively.

In this study, the most common clinical variant was chronic hyperkeratotic 16 (32%), followed by chronic interdigital 14 (28%), which differs from another study, where they found that chronic interdigital type was most common.<sup>20</sup>

Two groups of people were studied: group-A with terbinafine 250 mg daily and group B with itraconazole 200 mg daily for 14 days. We evaluated weekly during treatment and 02 weeks after cessation of therapy, and finally, on 08<sup>th</sup> week to see the clinical improvement and adverse effects. The clinical response was rated marked improvement (>75%), significant improvement (over 50%. <75%), moderate improvement (<50%), and no change or mild improvement. The clinical response was found in chronic hyperkeratotic: 08/08, 08/08; chronic intertriginous type: 07/07, 07/06; vesico-bullous, type: 06/05, 06/05; Mixed type: 04/03, 03/02 in group-A and group-B respectively. On average, 92% clinical improvement was found in group-A and 84% in group B. Keysen De et al.<sup>21</sup> compared two weeks of terbinafine at 250 mg/day to 2 weeks of itraconazole at 100 mg/day in tinea pedis; they found terbinafine superior to itraconazole for

clinical cure (94% vs. 72.4%). Iwao Takinchi et al.<sup>22</sup> studied and found 89.3% improvement in tinea pedis with one week of treatment with 250 mg terbinafine. A study by Barnatson et al.<sup>22</sup> found 72% improvement with 250 mg of terbinafine for one week in tinea pedis. Hay et al.<sup>23</sup> compared two weeks of oral terbinafine (250mg/day) with four weeks of oral itraconazole (100mg/ day), and the cure of the terbinafine group was 78% in tinea pedis. So, comparing the other studies with our study revealed that some of the studies are consistent with our result, and some are slightly different from ours.

In this current series, it was observed that most patients had nausea (20.0%) followed by 08% diarrhea in group A. On the other hand, in group B, most patients had nausea (28.0%), followed by 4.0% fatigue and 4.0% diarrhea, and only 01 patient found elevated liver enzyme but did not exceed the upper limit. The side-effects were mild and tolerable in the terbinafine group obtained by.<sup>26</sup> Eighty percent of patients in the terbinafine group had transient, mild to moderate nausea. None of the patients in any group discontinued the treatment because of the drug's adverse effects. It is important to mention that side effects were minimal in both groups of patients observed by Sen et al.

## Conclusion

This study was undertaken to compare the efficacy and safety of terbinafine vs. itraconazole in treating tinea pedis. Both drugs significantly improved the disease, without significant difference, at least eight weeks after follow-up. Furthermore, both drugs are well tolerated in the short courses of treatment. Terbinafine may represent a good alternative in treating tinea pedis in patients unable to take itraconazole or other available drugs due to contraindication or toxicity.

**Conflict of interest:** None declared

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All correspondence to  
**Lt Col Md Humayun Kabir**,  
 Classified dermatologist,  
 Combined Military Hospital (CMH), Dhaka.  
 E-mail : humayun 1087@yahoo.com