Efficacy of Voriconazole Versus Itraconazole in the Treatment of Dermatophyte Infections

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ABSTRACT

Background: Dermatophyte infections, commonly referred to as tinea or ringworm, are superficial fungal diseases that involve keratinized tissues such as the skin, hair, and nails. Their pathogenesis is linked to fungal adhesion, tissue penetration, and host inflammatory responses. Several antifungal agents are used in treatment, including terbinafine, griseofulvin, fluconazole, and itraconazole. Voriconazole, a second-generation triazole with broad-spectrum activity, inhibits fungal cytochrome P450–dependent 14-α-lanosterol demethylation, disrupting cell membrane integrity. Itraconazole, another triazole, also interferes with ergosterol synthesis via cytochrome P450 inhibition and has been widely applied in dermatophytosis management.

Objectives: To compare the therapeutic efficacy of voriconazole and itraconazole in patients with dermatophyte infections.

Methods: This quasi-experimental study was conducted in Department of Dermatology & Venerelogy, Combined Military Hospital (CMH), Sylhet. Total 100 patients aged between 15 to 70 years, with recurrent and chronic dermatophyte infections all over the body, except those who have not responded to conventional antifungals taken for almost 4 weeks were enrolled for study. Then subjects were allocated in to two group- Group-A (patients treated by oral voriconazole 200mg twice daily) and Group-B (patients treated with oral itraconazole 100mg twice daily). Then treatment outcome was compared. All information was recorded in data collection sheet. Data was processed and analysed with the help of computer program SPSS and Microsoft excel.

Result: The mean age of participants was 34.1 ± 6.2 years in Group A and 32.9 ± 6.1 years in Group B. Males comprised 80% of Group A and 60% of Group B, with no significant differences in age or sex distribution between groups ($p > 0.05$). Complete clinical cure was observed in 72% of patients treated with voriconazole compared to 44% in the itraconazole group. This difference was statistically significant ($p = 0.001$).

Conclusions: Voriconazole demonstrated superior efficacy compared to itraconazole in the management of dermatophyte infections. It appears to be a safe and effective oral antifungal option for patients with chronic or resistant disease.

Keywords: Fungal Skin Disease, Dermatophytosis, Ringworm, Voriconazole, Itraconazole, Antifungal agents

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INTRODUCTION

Fungal skin diseases (FSD) are among the most prevalent infections worldwide, affecting nearly one billion individuals. According to the Global Burden of Disease (GBD) 2019 estimates, approximately 1.65 billion people were living with FSD, with an age-standardized prevalence rate (ASPR) of 21.4% and an incidence rate (ASIR) of 21.2%, underscoring their substantial public health impact.[1] The majority of cases are attributed to dermatophytes, particularly species belonging to the genera *Trichophyton* and *Microsporum*.*2, 3*

Fungal skin diseases or dermatophyte infections, collectively termed "tinea," are transmitted through direct human-to-human contact (anthropophilic species), exposure to animals (zoophilic species), or from contaminated soil (geophilic species). Indirect transmission via fomites such as clothing, footwear, or personal items is also common.[4, 5] Clinical diagnosis is usually based on examination, but ancillary tools such as Wood's lamp, fungal culture, or histopathology may be employed when necessary.

Tinea that infect humans are classified into nine genera, although only *Trichophyton*, *Epidermophyton*, and *Microsporum* are clinically significant. Based on the anatomical site, infections are categorized as tinea capitis (scalp), tinea faciei (face), tinea barbae (beard), tinea corporis (body), tinea manuum (hand), tinea cruris (groin), tinea pedis (foot), and tinea unguium (nails).[6, 7] Despite being non–life-threatening, dermatophytosis is associated with considerable morbidity, particularly due to chronicity, relapses, and it ultimately impaired quality of life[8]. Environmental factors such as hot and humid climates, increased urbanization, and lifestyle practices like the use of occlusive footwear and tight clothing contribute to its high prevalence of tines infection in tropical regions. Furthermore, recent studies, especially from India, indicate a changing epidemiological pattern, with an increased predominance of *T. mentagrophytes* complex over *T. rubrum*, coupled with rising antifungal resistance.[9, 10]

Current therapeutic options include topical agents for limited disease and systemic agents for extensive or refractory cases. Terbinafine and itraconazole remain the most frequently prescribed oral antifungals. Terbinafine inhibits squalene epoxidase, an enzyme essential for ergosterol synthesis, thereby exerting fungicidal effects.[11] Itraconazole, a triazole derivative, blocks fungal cytochrome P450–dependent 14-α-demethylase, disrupting ergosterol production.[12] Both drugs have shown significant clinical utility, but reports of incomplete cure and frequent relapses are increasingly recognized.[13, 14] Resistance linked to genetic and environmental adaptations of dermatophytes has further complicated treatment.

Voriconazole, a second-generation triazole antifungal available in both oral and intravenous forms, exhibits broad-spectrum activity and has shown efficacy against strains resistant to fluconazole and terbinafine.[15] The British Association of Dermatologists acknowledges voriconazole as a potential alternative in refractory dermatophytosis and in cases unresponsive to standard regimens.[16] Clinical studies among 200 cases reported the efficacy was 82%.[17] Another study reported that resistance against fluconazole (85.3%) and terbinafine (58.0%) was high, compared to voriconazole (5.0%). Voriconazole seems to be more effective and safer against dermatophytosis.[18]

In another study voriconazole (group-A) and itraconazole (group-B) were compared. Result shows that voriconazole achieved 84.2% complete clearance and 15.8% of the participants achieved partial response to the treatment. But

patients who received itraconazole, 15.7% showed complete response, 42.1% partial cure and 42.2% patients did not show any improvement after the treatment. It is safe to conclude, that voriconazole shows better efficacy and results in treating resistant dermatophyte infections.[19] Similar study reported that resistance against fluconazole and terbinafine was most common in the, 85.33% and 58% respectively. Voriconazole is seems to be more effective against dermatophytes. No resistance against voriconazole was observed.[20]

Given the rising burden of resistant dermatophytosis and the limitations of conventional antifungals, there is a growing need to evaluate newer alternatives. This study was therefore designed to compare the efficacy of voriconazole with itraconazole in the treatment of dermatophyte infections.

MATERIALS & METHODS

This quasi-experimental study was conducted in Department of Dermatology, Combined Military Hospital (CMH), Jalalabad Cantt, Sylhet, over a period of six months. A total of 100 patients were enrolled in this study. Inclusion criteria consisted of patients that aged between 15 to 70 years, with recurrent and chronic dermatophyte infections, all over the body, except those who have not responded to conventional antifungals, taken for almost 4 weeks. Chronic infection is defined that has been present for more than 6 months, with proper treatment been taken. Recurrent infections are the ones in which symptoms reappear within 6 weeks of clinical cure or stopping of the treatment. Patients of age less than 15 or greater than 70 years, with infections on the scalp, i.e., Tinea capitis and involving the nails, i.e., tinea unguum, with deranged lipid profile, liver functions or renal function tests, pregnant females, or breastfeeding mothers were excluded from the study. A written informed consent was taken from all the participants of the study. The patients were divided into two groups, Group A, (50 patients) who were treated with oral voriconazole 200mg twice daily and Group B, (50 patients) treated with oral itraconazole 100mg twice daily. They were given treatment for a period of 4weeks or earlier, in patients if complete response is achieved. Patients were followed up at 2 weeks, 4 weeks, after completion of the treatment.

Clinical response assessment: Clinical assessment was done before the treatment, and four weeks after the completion of the course of treatment. Thorough cutaneous examination and mycological assessments was performed in each patient and at each follow up visit. Clinical responses were observed in various clinical sign and symptoms such pruritus, scaling and erythema were rated according to a 4-point assessment scale of 0-3 (0=absent, 1= mild, 2=moderate, 3= severe)[15, 21, 22]. Patients were checked for residual changes or recurrence two weeks; four weeks (after treatment ended).

Efficacy[19]: Efficacy is classified as

- Complete response or cure: It means 100% cure, which indicate that all the lesions healed completely (or absence of scaling, erythema and pruritus) with negative KOH (Potassium hydroxide).
- Partial response, in which there is a cure in >50% or more than half of the total lesions with negative KOH. It means persistence of moderate clinical symptoms, but negative KOH microscopic examination.
- Failure or no response: In which no or minimal improvement of clinical symptom and microscopy is still positive.

Data were entered and analyzed by the Statistical analysis for Special Sciences 23. The qualitative variables represented as frequencies and percentages, while the quantitative variables presented as mean ±SD.

RESULTS

TABLE-I: Distribution of the study patients by age (n=100)

Age (In year)	Group A (50)	Group B (50)	Significance
15-30	14 (28.0%)	13 (26.0%)	x^2=0.857, df=3, p=0.087
31-45	25 (50.0%)	22 (44.0%)	
46-60	9 (18.0%)	12 (24.0%)	
>60	2 (4.0%)	3 (6.0%)	
Mean±SD	34.1±6.2	32.9±6.1	t=0.976, p=0.332

In the 15-30 years age group, 14 respondents (28.0%) belonged to group A and 13 respondents (26.0%) belonged to group B. In the 31-45 years age group, group A had 25 respondents (50.0%), group B had 22 respondents (44.0%). In the 46-60 years age group, 9 respondents (18.0%) were in group A and 12 respondents (24.0%) were in group B. Among those >60 years age, group A had 2 respondents (4.0%) and group B had 3 respondents (6.0%). Age distribution did not differ significantly between Group A and Group B, meaning the two groups were comparable by age. Mean age was found to be 34.1 with SD 6.2 in Group A and 32.9 with SD 6.1 in Group B. there is no statistically significant in mean age between Group A and Group B. This means the group are comparable in age, and age is not a confounding factor in this study.

TABLE-II: Distribution of the patients according to treatment group and sex (n=100)

Treatment group	Male	Female	Total	Significance
Group A	40 (80.0%)	10 (20.0%)	50 (100.0%)	x^2=4.762, df=1, p=0.029
Group B	30 (60.0%)	20 (40.0%)	50 (100.0%)	
Total	70 (70.0%0	30 (30.0%0	100 (100.0%)	

Table II shows sex distribution of the study patients, it was observed that majority 40(80.0%) patients were male in group A and 30(60.0%) in group B. There is significant association [x^2=4.762, df=1, p=0.029] between two groups.

Figure-I: Distribution of the patients according to treatment group and sex (n=100)

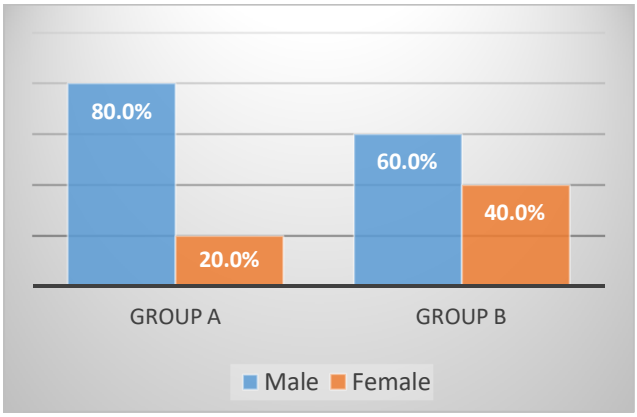


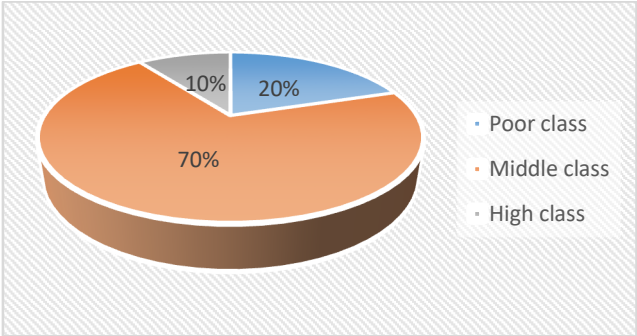
Fig-1 show sex distribution. In Group A, 40 patients (80.0%) were male and 10 patients (20.0%) were female. On the other hand, in group B, 30 patients (60.0%) were male and 20 patients (40.0%) were female. A chi-square test was performed to assess the association between treatment group and sex. The test result was x^2=4.762 with 1 degree of freedom and p=0.029, indicating a statistically significant association between treatment group and sex at the 5% level.

TABLE-III: Family history of dermatophyte infection (n=100)

Family History	Group A (50)	Group B (50)	Significance
Yes	14 (28.0%)	14 (28.0%)	x^2=0.000, df=1, p=1.000
No	36 (72.0%)	36 (72.0%)	
Total	50 (100.0%)	50 (100.0%)	

In group A and group B, 14 respondents (28.0%) had family history of dermatophyte infection and rest 36 respondents (72.0%) had no family history of dermatophyte infection. Family history did not differ significantly between Group A and Group B, meaning the two groups were comparable by family history.

Fig-2: Socioeconomic status of the study population (n=100)



Socioeconomically middle class (70.0%) comprising the major percentage of the patients (Figure II).

TABLE-IV: Clinical profile of the respondents (n=100)

Clinical profile	Group A (50)	Group B (50)	Significance
Form of illness			x^2=0.019, df=1, p=0.890
Mild	2 (4.0%)	1 (2.0%)	
Moderate	14 (28.0%)	14 (28.0%)	
Severe	34 (68.0%)	35 (70.0%)	
Duration of lesion			x^2=0.176, df=1, p=0.675
Less than 6 months	7 (14.0%)	5 (10.0%)	
6 months to 1 years	31 (62.0%)	32 (64.0%)	
More than 1 years	12 (24.0%)	13 (26.0%)	

Mild form of illness detected in 2 respondents (4.0%) in group A and 1 respondent (2.0%) in group B. Moderate illness found in 14 respondents (28.0%) in group A and group B respectively. Severe form of illness had 34 respondents (68.0%) in group A and 35 respondent (70.0%) in group B. Illness distribution did not differ significantly between Group A and Group B, meaning the two groups were comparable by form of illness. Duration of lesion revealed that, 7 respondents (14.0%) in group A and 5 respondent (10.0%) in group B had less than 6 months duration. Followed by 6 months to 1 year duration found in 31 respondents (62.0%) in group A and 32 respondent (64.0%) in group B and more than 1 years found in 12 respondents (24.0%) in group A and 13 respondent (26.0%) in group B. There is no statistically significant in duration of illness between Group A and Group B, this means the group are comparable in disease duration.

Fig-3: Types of dermatophytosis (n=100)

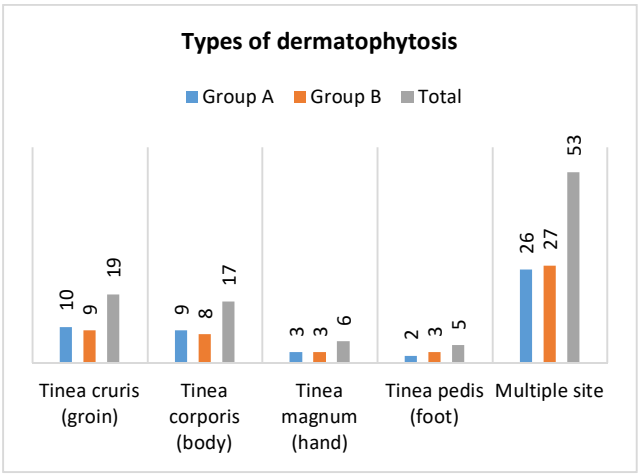


Figure III shows the distribution of the patients by of clinical types of dermatophytosis. Among the 100 patients, tinea cruris was found in total 19 patients [10(20%) in group A and 9(18%) in group B]. Tinea corporis was found in total 17 patients [9(18%) in group A and 8(16%) in group B]. Tinea magnum was found in total 6patients [3(6%) in group A and B respectively]. Tinea pedis was found in total 5patients [2(4.0%) in group A and 3(6.0%) in group B]. In this study maximum patients had multiple site of involvement.

TABLE-V: Distribution of the patient by clinical response of therapy (n=100)

Clinical parameters	Group A (n=50)				Group B (n=50)				P value
	no	Mild	Moderate	Severe	no	Mild	Moderate	Severe	
Erythema									-
Baseline	0	2(4.0)	13(26.0)	35(70.0)	0	1(2.0)	12(24.0)	37(74.0)	0.685
First FU	34(68.0)	13(26.0)	3(6.0)	0	23(46.0)	17(34.0)	10(20.0)	0	0.921
Final FU	42(84.0)	8(16.0)	0	0	32(64.0)	11(22.0)	7(14.0)	0	0.042
Scaling									
Baseline	0	10(20.0)	36(72.0)	4(8.0)	0	12(24.0)	33(66.0)	5(10.0)	0.842
First FU	36(72.0)	9(18.0)	5(10.0)	0	21(42.0)	16(32.0)	12(24.0)	1(2.0)	0.035
Final FU	48(96.0)	2(4.0)	0	0	30(60.0)	11(22.0)	9(18.0)	0	0.021
Pruritus									
Baseline	0	3(6.0)	47(94.0)	0	0	5(10.0)	45(90.0)	0	0.811
First FU	18(36.0)	25(50.0)	7(14.0)	0	25(50.0)	18(36.0)	7(14.0)	0	0.177
Final FU	39(78.0)	9(18.0)	2(4.0)	0	30(60.0)	16(32.0)	4(8.0)	0	0.026

Table V shows clinical response of therapy. At baseline, moderate to severe scores for erythema, scaling and pruritus were noted in 48(96.0%), 40 (80.0%) and 47(94.0%) of patients in Group A and 49(98.0%), 38(76.0%) and 45(90.0%) of patients in group B. Statistically, there was no significant difference between two groups for symptom scores for all the three symptoms at baseline. Improvement in all the three symptoms (erythema, scaling and pruritus) was seen from the first follow-up to final follow up. No significant difference in pattern of resolution of all the three symptoms was observed between two groups at first follow up. By second or final follow up (4 weeks) resolution of symptoms erythema, scaling and pruritus seen in 84.0%, 96.0% and 78.0% of Group A patients and 64.0%, 60.0% and 60.0% of Group B patients. Statistically, there significantly better response to treatment in voriconazole group. The findings of the present study thus show that with respect to resolution of symptoms, Voriconazole had a slight edge over Itraconazole. Voriconazole tended to show a faster resolution of symptoms as compared to Itraconazole. After therapy, 78.0% participants in group A and 60.0% in group B with tinea infections were fully cured.

Fig-4: Frequency of adverse effects among the respondents (n=100)

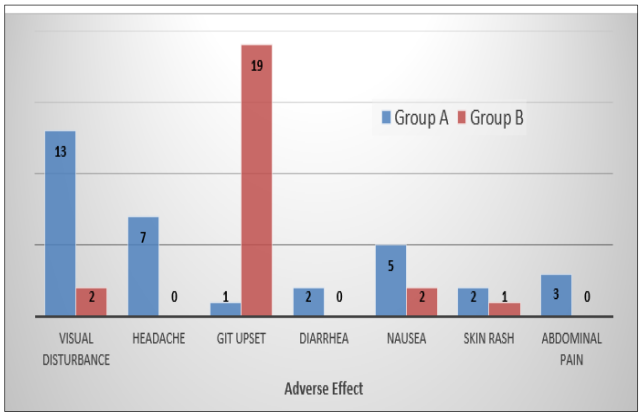


Figure IV shows the distribution of patient according to side effects associated with both drugs. About 12(24.0%) developed side effects and among them disturbance of vision was found in 13(26.0%) cases, followed by headache 7(14.0%) cases and nausea 5(10.0%), diarrhoea, abdominal pain, general weakness, etc. Adverse events from treatment with itraconazole was found in 20 patients with GIT upset was present in 19(38.0%) patient, followed by nausea in (4.0%), skin rash in 1(2.0%) cases.

TABLE-VI: Evaluation of efficacy of voriconazole and itraconazole among the respondents (n=100)

Overall treatment outcome	Group A (50)	Group B (50)	Significance
Complete cure	36 (72.0%)	22 (44.0%)	x^2=7.966, df=1, p=0.0048
Partial cure or improvement	14 (28.0%)	15 (30.0%)	
Failure or no response	0	13 (26.0%)	

Distribution of patients by clinical efficacy is shown in table VI. Complete cure (clinical cure + mycological cure) was seen in total 58 patients, partial cure or improvement (moderate clinical symptoms, but negative KOH microscopic examination) was seen in 29 patients and failure (no or minimal improvement of clinical symptom with positive KOH) in 13 patients. On comparison between groups significant outcome was observed in Group-A. Complete cure was achieved in 72.0% of the patients being treated with voriconazole (or Group A), whereas 44.0% patient treated with itraconazole (or Group B) was completely cured. The differences are statistically significant (p=0.001). It was found that 13 cases were failure to treatment and all of them were treated with itraconazole. So, treatment with voriconazole is better and effective in the means of complete cure rate. The difference was statistically significant ($p<0.05$) between groups.

DISCUSSION

In the present study, the majority of participants were in the younger and middle-aged groups, with 27%

aged 15–30 years and 47% aged 31–45 years. The mean age was comparable between treatment groups (34.1 ± 6.2 years in group A and 32.9 ± 6.1 years in group B), with no statistically significant difference ($p > 0.05$). Males were more commonly affected, representing 80% of group A and 60% of group B, although the gender distribution between the groups was not significant. Family history of tinea infection was observed in 28% of participants. These findings are consistent with earlier studies that also reported a male predominance and high prevalence among younger age groups.[15, 20, 23]

The clinical pattern and presentation of dermatophytosis has shifted in recent years, with increasing reports of chronicity, relapses, and reduced responsiveness to standard antifungals such as terbinafine and itraconazole. Environmental factors and pathogen adaptation have contributed to these changes, highlighting the urgent need for newer therapeutic strategies. Several investigators have demonstrated declining cure rates with conventional agents, while second-line drugs such as voriconazole have shown more promising outcomes. Voriconazole shows promising results clinically and mycologically.[19] No resistance of voriconazole was detected. Similar study observed that 88.5% of cases were fully cure and 11.5% partially cure with voriconazole which seems to be more effective against dermatophytes.[20]

In this study, the complete cure rate with voriconazole (72%) was significantly higher compared to itraconazole (44%), with treatment failures observed exclusively in the itraconazole group ($p = 0.001$). These findings suggest that voriconazole offers superior clinical and mycological clearance compared to itraconazole. Our results are in agreement with previous research, where voriconazole achieved complete clearance in 84–90% of cases.[15, 17, 19] In contrast, cure rates with itraconazole vary widely, with some studies reporting response rates as low as 15–20%, while others found higher success rates depending on patient population and resistance patterns.[19, 24, 25] This variability may reflect regional differences in species distribution and drug susceptibility.

Resistance to antifungal therapy is an emerging global concern. Reports from South Asia have documented high resistance rates to fluconazole (up to 85%) and terbinafine (50–60%), while resistance to itraconazole is also increasing.[20, 26, 27] In contrast, several studies have noted minimal or no resistance against voriconazole, making it a strong candidate for the management of recalcitrant dermatophytosis.[20, 27] Our findings reinforce this evidence, as voriconazole demonstrated higher efficacy and lower treatment failure compared with itraconazole.

Adverse effects were recorded in both treatment arms. In the voriconazole group, 24% of patients experienced side effects, most commonly transient visual disturbances (26%), followed by headache (14%) and gastrointestinal complaints such as nausea and abdominal pain (10%). Adverse events from treatment with itraconazole was found in 20 patients, gastrointestinal upset was most frequent (38%), with additional reports of nausea (4%) and skin rash (2%). These observations are comparable with earlier studies, which have described similar adverse events with voriconazole—particularly visual symptoms, photophobia, and headache—although these were generally self-limiting.[15, 19, 23] Itraconazole-related gastrointestinal intolerance has also been widely documented.[23, 26, 28] The relatively short treatment duration in our study may have contributed to the lower incidence and severity of adverse effects.

Taken together, our results highlight that voriconazole is not only more effective but also reasonably well tolerated compared to itraconazole. While some side effects were observed, they were generally mild and manageable. The overall benefit-to-risk ratio appears favorable for voriconazole, especially in resistant or relapsing cases. These findings align with recent reports emphasizing the importance of expanding the use of newer antifungals to address the growing problem of dermatophyte resistance.[26, 28]

CONCLUSIONS

Based on these observations, it is concluded that Voriconazole be considered as an effective treatment option for tinea infection. Side effects noticed in both groups, but it was self-limiting and subsided

spontaneously. No need for further treatment for side effects in both groups. Due to high temperature and increased humidity, there are increased cases of dermatophytosis and other fungal infections especially in Bangladesh. There was increased incidence of drug resistance observed over a period of time to the antimycotic drugs commonly used for the treatment i.e. fluconazole, terbinafine. We can conclude that Voriconazole is highly effective and well tolerated by patients and can be choice in the treatment of dermatophytosis. Due to better efficacy and results achieved with voriconazole, it is important that we use the drug judiciously so that the resistance does not occur, and it keeps on giving the same result in the coming years. More work is required in this regard worldwide.

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