

## Original article

## Efficacy and Safety of Voriconazole in the treatment of resistant cases of Dermatophytosis

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**Abstract:**

This is a descriptive type of longitudinal study conducted among Hundred clinically diagnosed cases of dermatophytes attending at skin out patients department of Zainul Haque Sikder Women's Medical College, Bangladesh from August 2018 to August 2019 to observe the efficacy and safety of voriconazole among the resistant cases of dermatophytosis. Among 100 patients, 40 were males and 60 females between ages 20 and 65 years of all age group with clinical, mycological diagnosis of dermatophytosis. To find out antifungal resistance pattern as well as efficacy and Safety of Voriconazole among dermatophytes. (Skin, hair and nail samples were taken aseptically. All patients were resistant against present treatment options like: fluconazole, itraconazole & terbinafine etc.) All patients were treated with Voriconazole. Duration of treatment of each patient was 4 weeks. Resistance against fluconazole and terbinafine was most common, 85.33% and 58% respectively. 5% resistance against voriconazole was observed in this study. Resistance against fluconazole was noted among all species of dermatophytes, followed by terbinafine. Among 100 patients 80% was fully cure and rest of 15 % were partially cure with 5% resistant of Voriconazole which is seems to be more effective and safer against dermatophytosis.

**Key words:** Resistant Dermatophytes, Antifungal, Efficacy, Safety, Voriconazole

**Introduction**

Dermatophytes are filamentous fungi that are able to digest and obtain nutrients from keratin, primarily a component of skin hair and nails. Cutaneous mycoses are mostly caused by keratinophilic filamentous fungi called dermatophytes and are classified into three genera: Trichophyton, Microsporum and Epidermophyton. So far, about 30 species of dermatophytes have been identified as human pathogens<sup>1</sup>. Although infections caused by dermatophytes are generally limited to the surface regions of the skin, these fungi can behave in a manner invasive, causing deeper and disseminated infection, especially in immunocompromised patients<sup>2</sup>. World Health Organization estimates dermatophytes affect about 25% of the world population<sup>3</sup>. Anthropophilic dermatophytes are associated with humans and rarely infect animals. Zoophilic dermatophytes cause infection in animals and may infect humans who come in contact. Geophilic dermatophytes are generally found in soil and take part in decomposition of hair, nails, feathers and horns<sup>4</sup>.

When the organism grows on the host, living tissue is not usually invaded. The organism simply colonizes the keratinized outermost layer of skin. The disease is known as tinea or ringworm. It is the result of the host reaction to the enzymes released by the fungus during its digestive process. Dermatophytes are the only fungi that have evolved a dependency on human or animal infection for the survival of the species. It is therefore these fungi are among the most common infectious agents<sup>5</sup>. The most common dermatophytes that causes cutaneous mycoses are Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum canis and Trichophyton tonsurans<sup>6</sup>. The tinea infections are prevalent worldwide but they are common in geographical areas with higher humidity. Overpopulation and poor hygienic living conditions also contribute to dermatophytic infections. Hot and humid climate of Bangladesh makes dermatophytosis a very common superficial fungal infection of skin<sup>7</sup>. In recent years, the number of human infections caused by this group of fungi has increased considerably

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and is of particular concern in immune compromised patients<sup>8</sup>. Studies conducted show that resistance among dermatophytes is not uncommon and fluconazole to be most resistant and voriconazole to be most sensitive drug for dermatophytes. Some investigators reported that the disease pattern of fungal infections varies among the different countries and different areas within the same country<sup>9,10</sup>. Due to high temperature and increased humidity, there are increased cases of dermatophytosis and terbinafine. Therefore, this study was carried out to find out incidence of dermatophytes infection as well as prevalence of drug resistance and the efficacy of Voriconazole to superficial fungal infection.

**Materials and Methods**

Hundred clinically diagnosed cases of dermatophytes, 40 males and 60 females between ages 20 and 65 years attending at skin out patients department of Zainul Haque Sikder Women’s Medical College, Bangladesh from August 2018 to August 2019 to observe the efficacy and safety of voriconazole among the resistant cases of dermatophytosis.

**Procedure of Treatment**

The patient of tinea infections was identified first. The diagnosis was made on the clinical basis by assessing morphology of lesions, Pruritus, age of onset and their distribution sites. To reach a clinical diagnosis detailed history and thorough physical examination done. Then clinical conditions of the patient were recorded. (by us) along with hematological and biochemical profile, like blood for total count, differential count, ESR, platelet count, random blood sugar, serum for ALT and serum creatinine level. Finally, all patients with tinea infections which is diagnosed clinically & mycologically were treated by oral Voriconazole 200 mg (available as Voricon 200mg tab) 1<sup>st</sup> day 400mg twice then from 2<sup>nd</sup> day onward 200 mg twice daily for 4 weeks. The cases were divided as None, mild form (itching, red and flaky skin), moderate form (moderate itching, thick, oily and yellow) and severe form (extensive itching, inflamed skin) and patient’s subjective assessment of pruritus and burning sensation were evaluated before and after treatment. A final medical assessment of efficacy and safety are made at the end of the treatment period using a four -point scale (categories: Fully cure 80%, moderately cure 15%, & 5% resistant) and the assessment result is recorded and analyzed to prepare the final result. Follow up were done at the end of 0, 1<sup>st</sup>, 2<sup>nd</sup>, & 4<sup>th</sup> week.

**Results**

The study was carried out for a period of total 12 months from August 2018 to July 2019 in the OPD at Zainul Haque Sikder Women’s Medical College, Bangladesh.

Total one hundred patients of tinea infections were selected. Among them, 20-35 years age group was 56%, 35-50 years was 33%- and 50-65-years age group was 11%, regarding sex, (36%) males and (64%) females between 20-65 years aged patients with tinea infections (Table I).

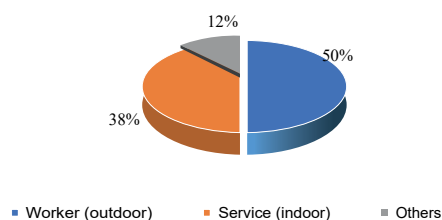
**Table 1: Incidence at age of onset and sex distribution (n=100)**

Age at onset	Male (%)	Female (%)	Overall (n-100)
>20-35	25 (45.69)	31 (55.37)	56
35-50	6 (17.32)	27 (82.27)	33
50-65	5 (46.76)	6 (51.96)	11
Total	36	64	100

**Table 2: Distribution of epidemiological profile (n=100)**

Epidemiological profile	Frequency
Married	
Yes	70 %
No	30 %
Family History	
Yes	17 %
No	83 %

In table II among one hundred infected patients 70% are married whereas number of unmarried is 30%. Regarding family history, (17%) had positive family history and (83%) had negative family history of tinea infections. Regarding occupation among the patients, 50% were outdoor worker, 38% were involved in indoor service and rest 12% involved in other occupation (Figure I)



**Fig 1: Distribution of respondents according to occupation**

**Table 3: Distribution of the patient by severity of disease, duration of lesions, and site of lesions (n=100).**

Parameters Different forms	Frequency
Mild	2%
Moderate	15%
Severe	83%
Duration of lesion	
Less than 6 months	8%
6 months to 1 years	90%
More than 2 years	2%
Site of lesion (multiple response may exceed hundred)	38%
Tinea cruris (groin)	25%
Tinea corporis (body)	15%
Tinea magnum (hand)	12%
Tinea pedis (foot)	10%
Tinea versicolor (various colors)	

**Table-4: Distribution of the patient by response of therapy at the end of the study (n=100)**

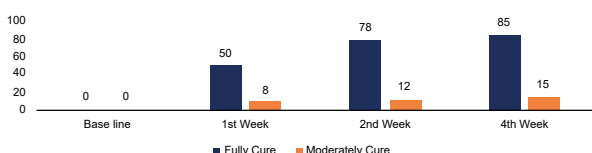
Form of different tinea infections	Fully cure	Moderately cure
Mild (2%)		0%
Moderate (15%)	2%	0%
Severe (83%)	15%	15%
Total (100)	85%	15%

Table 5 showed that 85% patients of different tinea infections had fully cure, only 15% moderately cure. 15% severe patients were moderately cure and they need to increase the duration.

**Table 6: Incidence of side effects of Voriconazole occurred during the treatment (n=100)**

Side effects	Number	Percentage (%)
Rash	3	3.0 %
Headache	5	5.0 %
Vertigo	10	10.0 %
Blurring Vision	30	30.0 %
Total	48	48.0 %

Table 5: showed that only 48 % seen with side-effect like rash 3% rash, 5% headache, vertigo 10%, Blurring Vision 30%. 2 patients have hypersensitivity & discontinue treatment.



**Figure 2: Response of treatment with voriconazole by duration (n=100)**

**Discussion:**

The study was carried out for a period of total 12 months from August 2018 to July 2019 in the OPD at Zainul Haque Sikder Women’s Medical College, Bangladesh. Total one hundred patients of different tinea infections were selected. In table I 20-35 years age group was 56%, 35-50 years was 33%- and 50-65-years age group was 11%, regarding sex, (36%) males and (64%) females between 20-65 years aged patients with tinea infections. In table II among one hundred infected patients 70% are married whereas number of unmarried is 30%. Regarding family history, (17%) had positive family history and (83%) had negative family history of tinea infections. In figure I: Regarding occupation among the patients, 50% were outdoor worker, 38% were involved in indoor service and rest 12% involved in other occupation. Among the one hundred patients of different tinea infections in table II, mild form was 2%, moderate was 15% and severe was 83%. % Regarding duration of lesions, most of the cases 90% duration was in between 6 months to 1 years, and 8% was less than 6 month and rest of 2% was more than 2 years. Regarding site of lesions, maximum patients of different tinea infections 38% had involvement of groin, next 25% had involvement in the body, 15% had involvement in hand, 12% & 10% are respectively foot and others etc. . Fifty percent of total patients are outdoor worker used to exposure in sunlight and hot humid climate for their nature of occupation. This reflects the precipitating factor of tinea infections. The study showed that 85% patients of different tinea infections had very good response, only 15% patients were moderately cure of tinea infections and 5% patients found in resistant to Voriconazole. The efficacy of oral antifungals was attributable to their antifungal and/or anti-inflammatory effects by Gupta, Nicol and Batra 8. At present, systemic use of fluconazole, ketoconazole, itraconazole, and terbinafine has been associated with very low clinical response in the treatment of different tinea infections because of their narrow spectrum as well as high resistance rate. However, the efficacy of oral voriconazole which was highly effective against a greater spectrum of dermatophytes causes tinea infections and showed marked improvement. In one study, oral voriconazole first day 400 mg twice and from 2<sup>nd</sup> day 200 mg twice daily for 4 weeks. This dosage was chosen because it has been used effectively and safely in the treatment of different tinea infections. The study showed (Figure II) showed that improvement of fully cure group is 50% observed and moderately cure group 8% improvement on the 1<sup>st</sup> follow up visit at the 1<sup>st</sup> week. On the 2<sup>nd</sup> follow up visit at 2<sup>nd</sup> week, 78% cure of fully cure group and 12% cure of moderately cure group. Then 85% cure of fully cure group as well as 15%

moderately cure group at 4th week. The safety profile of voriconazole when used on a long-term basis, its efficacy against dermatophytes causes tinea infections, make voriconazole an excellent therapeutic option in different superficial fungal infections and treatment of choice in 'recalcitrant cases' of tinea infections. Our study had several limitations. First, no fungal culture was performed and the clinical outcome could not therefore be correlated with *Malassezia* yeast colonization. Consequently, a possible anti-inflammatory effect of voriconazole could not be evaluated. In addition, the self-remitting course of the disease, the number of patients and the duration of treatment in this study may have been insufficient to evaluate drug-related improvement. The current study was an attempt to develop a short, convenient, and safe treatment protocol, which is strongly needed for different tinea infections. The results of this study indicate that voriconazole is a suitable treatment for the patients of different superficial fungal infections like tinea and others. However, larger studies using different dosages and durations of therapy may provide a rationale for systemic use of voriconazole in different superficial fungal infections.

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