

Efficacy and Safety of Voriconazole in Patients with Dermatophytes

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ABSTRACT

Background: Dermatophytosis known as ringworm, is a fungal infection of the skin. It results in a red, itchy, scaly, circular rash. Hair loss may occur in the area affected. Aim of the study: The aim of this study was to find out incidence of dermatophytes infection as well as prevalence of drug resistance and the efficacy of Voriconazole to superficial fungal infection. **Methods:** A study was conducted at Upazilla Health Complex, Fulpur, Mymensingh during the period from January 2019 to November 2019. The study included 250 patients with clinical diagnosis of dermatophytosis. To find out antifungal resistance pattern and efficacy of Voriconazole among dermatophytes (Skin, hair and nail samples were taken aseptically. Some patients were resistant against present treatment options like: fluconazole, itraconazole & terbinafine etc.) All patients were treated with Voriconazole (Voricon used as a Voriconazole which was from a renowned pharmaceutical in Bangladesh name General pharmaceutical limited. Duration of treatment of each patient was 12 weeks. **Results:** Resistance against fluconazole and terbinafine was most common in the study, 85.33% and 58% respectively. Among the patients 88.4% was fully cured and rest of 11.6% were partially cured with Voriconazole which is seems to be more effective against dermatophytes. **Conclusion:** No resistance against voriconazole was observed in this study. Resistance against fluconazole was noted among all species of dermatophytes, followed by terbinafine. Fluconazole was least effective drug followed by terbinafine.

Keywords: Dermatophytes, Antifungal, Efficacy, Voriconazole.

INTRODUCTION

Dermatophytes also known as tineae or ringworm are fungi that require keratin for growth which attack the skin, hair, and nails in humans.^[1] Dermatophytes are a closely related group of fungi in 3 anamorphic genera of Trichophyton, Microsporum and Epidermophyton that originate from humans, different animals or soil. Except for a few systemic diseases and immunosuppressed patients.^[2-5] World Health Organization estimates that dermatophytes affect about 25% of the world population.^[6] 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.^[7] 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.^[8] The most common dermatophytes that cause cutaneous mycoses are Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum canis and Trichophyton tonsurans.^[9] 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.^[10] In recent years, the number of human infections caused by this group of fungi has increased considerably and is of particular concern in immune compromised patients.^[11] 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.^[12,13] Due to high temperature and increased humidity, there are increased cases of dermatophytosis and other fungal infections especially in Bangladesh. Since 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, itraconazole and terbinafine. Therefore, this study was carried out to find out incidence of dermatophytes infection as well

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as prevalence of drug resistance and the efficacy of Voriconazole to superficial fungalinfection.

Objectives

- To find out the role of voriconazole in different tinea infections in Bangladesh

MATERIALS AND METHODS

Out of total tinea infected patients we selected only those patients who didn't respond to routine treatment, relapsed soon after stoppage of treatment or those having persistent dermatophytic infection. A total of five hundred patients of all age group and both sexes attending skin outpatient department were recruited into the study. The interventional study was carried out at Upazilla Health Complex, Fulpur, Mymensingh during the period from January 2019 to November 2019. Two hundred and fifty (250) patients of tinea infections were selected considering exclusion criteria like patients with known hypersensitivity to any ingredients of Voriconazole, Pregnancy/lactation, impaired hepatic function, impaired renal function and severe systemic illness. All the clinically suspected 250 cases were subjected to mycological work up. Purposive type non-probability sampling technique was followed in this study. After collection of data, these were screened by checking consistency, edited and were finally analyzed by software SPSS version-20.

Procedure of Treatment

The patient of tinea infections was identified first. The diagnosis was made on the clinical basis by assessing morphology of lesions, 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 were treated by oral Voriconazole 200 mg(available as Voricon 200mg tab) twice daily for 4 weeks. The cases were divided as mild from (itching, red and flaky skin), moderate form (moderate itching, thick, oily and yellow) and severe from (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 is made at the end of the treatment period using a four - point scale (categories: Fully cure 88.4%, moderately cure 11.6%) and the assessment result is recorded and analyzed to prepare the final result. Follow up were done at the end of 2nd, 4th, 8th, & 12th week.

RESULTS

Table 1: Distribution of the patient by epidemiological profile (n=250)

Components		n	%
Age (In years)	20-30	77	30.8
	31-40	145	58
	41-50	28	11.2
Sex	Male	145	58
	Female	105	42
Family history	Positive	57	22.8
	Negative	193	77.2

Table 2: Distribution of the patient by different form of disease, duration of lesions and site of lesions (n=250).

Components		n	%
Different forms	Mild	30	12
	Moderate	170	68
	Severe	50	20
Duration of lesion	Less than 6 months	20	8
	6 months to 1 years	127	50.8
	6 months to 1 years	90	36
	More than 2 years	13	5.2
Site of lesion	Tinea cruris (groin)	100	40
	Tinea corporis (body)	55	22
	Tinea magnum (hand)	37	14.8
	Tinea pedis (foot)	33	13.2
	Tinea versicolor (various colors)	25	10

Table 3: Distribution of the patient by response of therapy at the end of the study (n=250)

Form of different tinea infections	Fully cure	Moderately cure
Mild	12%	0%
Moderate	45.2%	0%
Severe	31.2%	11.6%
Total	88.4%	11.6%

Table 4: Distribution of the patients by side effect (n=250)

Side effects	n	%
Rash	8	3.2
Jaundice	11	4.4
Visual disturbances	10	4
Fever	7	2.8
Nausea	23	9.2
Vomiting	16	6.4
Diarrhoea	5	2
Headache	9	3.6
Total	89	35.6

Total two hundred and fifty patients of tinea infections were selected. Among them, 31-40 years age group was 58%, 20-30 years was 30.8% and 41-50-years age group was 11.2%, regarding sex, (58%) males and (42%) females between 20-50 years aged participants with tinea infections and regarding family history, (22.8%) had positive family history and (77.2%) had negative family history of tinea infections [Table 1]. Regarding occupation among the participants, 50.5% were outdoor worker, 37% were involved in indoor service and rest 12.5% involved in other occupation [Figure 1]. One hundred and seventy (68%) participants were moderately affected by the disease, fifty (20%) participants were severely affected and thirty (12%) participants were mildly

affected. For most of the participants (50.8%), the duration of the lesion was 6 months to 1 year. For most of the participants (40%), the lesion was sited in tinea cruris [Table 2]. After therapy, 88.4% participants with tinea infections were fully cured and 11.6% were moderately cured, where 45.2% were cured from moderate infection, 31.2% from severe infection and 12% from mild infection [Table 3]. Total eighty-nine (35.6%) participants had side effects after therapy, where twenty-three (9.2%) had nausea, sixteen (6.4%) had vomiting, eleven (4.4%) had jaundice, 10 (4%) had visual disturbances, nine (3.6%) had headache, eight (3.2%) had rash, seven (2.8%) had fever and five (2%) had diarrhoea [Table 4]. The study showed that improvement of fully cure group is 38% observed and moderately cure group 27.2% improvement on the 1st follow up visit at the 2nd week. On the 2nd follow up visit at 4th week, 75.2% cure of fully cure group and 53.2% cure of moderately cure group. Then 88% cure of fully cure group as well as 78% moderately cure group at 3rd week, at 4th week 100% cure found in fully cure group and 98% observed in moderately cure group [Figure 2].

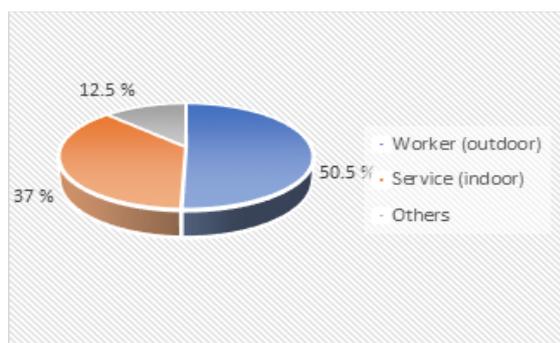


Figure 1: Distribution of patients according to occupation.

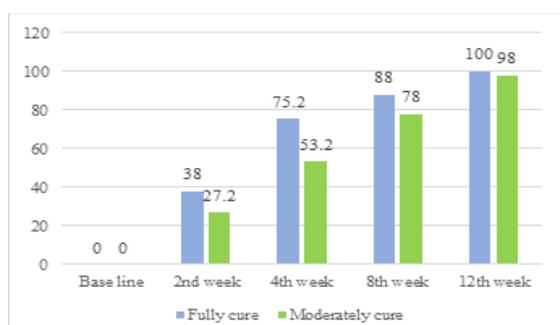


Figure 2: Distribution of the patient by follow up after voriconazole therapy

DISCUSSION

In our study, among two hundred and fifty participants, most study people (58%) were in the age group of 31-40 years, followed by 30.8% in 20-30 years and 11.2% in 41-50-years age group. In another study of Kafi MA. et al,^[14] among 100 study people

most study people (56%) were from 20-30 age group. Regarding sex, (58%) males and (42%) females between 20-50 years aged participants with tinea infections. Similar results found in another study of Ebert A et al,^[15] where from consistent clinical data among 226 study people 59% was male and 41% was female. Regarding family history, 22.8% had positive family history and 77.2% had negative family history of tinea infections. Similar results found in the study of Kafi MA et al,^[14] where among 100 study people 17% had family history and 83% did not have any family history of tinea infections. Regarding occupation among the participants, 50.5% were outdoor worker, 37% were involved in indoor service and rest 12.5% involved in other occupation. Similar results found in the study of Kafi MA et al,^[14] where among 100 study people 50% were outdoor worker, 38% were involved in indoor service and rest 12% involved in other occupation. One hundred and seventy (68%) participants were moderately affected by the disease, fifty (20%) participants were severely affected and thirty (12%) participants were mildly affected. In the study of Kafi MA et al,^[14] among 100 study people one hundred patients of different tinea infections in [Table 2], mild form was 2%, moderate was 15% and severe was 83%. For most of the participants (50.8%), the duration of the lesion was 6 months to 1 year. For most of the participants (40%), the lesion was sited in tinea cruris. After therapy, 88.4% participants with tinea infections were fully cured and 11.6% were moderately cured, where 45.2% were cured from moderate infection, 31.2% from severe infection and 12% from mild infection but there was no resistance to Voriconazole. In the study of Kafi MA et al,^[14] among 100 study people 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. Total eighty-nine (35.6%) participants had side effects after therapy, where twenty-three (9.2%) had nausea, sixteen (6.4%) had vomiting, eleven (4.4%) had jaundice, 10 (4%) had visual disturbances, nine (3.6%) had headache, eight (3.2%) had rash, seven (2.8%) had fever and five (2%) had diarrhoea. The study showed that improvement of fully cure group is 38% observed and moderately cure group 27.2% improvement on the 1st follow up visit at the 2nd week. On the 2nd follow up visit at 4th week, 75.2% cure of fully cure group and 53.2% cure of moderately cure group. Then 88% cure of fully cure group as well as 78% moderately cure group at 3rd week, at 4th week 100% cure found in fully cure group and 98% observed in moderately cure group.

CONCLUSION

In our study no resistance against voriconazole was found whereas resistance against fluconazole was noted among all species of dermatophytes, followed

by terbinafine. Among all the study people 88.5% were fully cure and rest of 11.5% were partially cure with voriconazole which seems to be more effective against dermatophytes.

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