

Original Article



Comparison of Efficacy of Single Oral Dose Fluconazole Versus Single Oral Dose Itraconazole in Patients with Pityriasis Versicolor

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ABSTRACT

Objective: To compare the efficacy of single oral dose Fluconazole and Itraconazole in patients with Pityriasis Versicolor.

Methodology: This Randomized control trial study was conducted at the Department of Dermatology, Combined Military Hospital, Abbottabad, Pakistan from March 2022 to August 2022. A total of 60 patients coming to OPD of derma department and diagnosed with Tinea Versicolor were randomized in 2 equal groups of 30 patients each. Patients diagnosed on odd serial number were allocated to group A and were prescribed oral Fluconazole (400 mg stat) while patients diagnosed on even serial number were allocated to group B and were prescribed oral Itraconazole (1000 mg stat). Diagnosis was made clinically and then by using mycological tests. Follow up visits were made at completion of 2nd and 4th weeks of start of treatment. Primary outcome was set as efficacy of the treatments at completion of 4 weeks that was assessed using mycological tests.

Results: In this study, age ranged was from 19 to 40 years with mean age of 30.066 ± 7.74 years. Mean duration of disease was 4.216 ± 1.29 months. At completion of study (4 weeks), treatment was effective in 25 patients (83.33%) in group A while in 17 patients (56.6%) in group B with a significant difference in efficacy between two groups ($p=0.024$).

There was a good tolerability in both groups without any serious adverse reactions reported.

Conclusion: Single oral dose of Fluconazole is more effective compared to single oral dose of Itraconazole in the treatment of Pityriasis Versicolor.

Keywords: Itraconazole, Fluconazole, Pityriasis versicolor.

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Introduction

Pityriasis versicolor (PV) also called Tinea Versicolor is a common superficial chronic fungal infection of the skin caused by species of lipophilic yeast known as *Malassezia* species. The yeast is proliferated in the stratum corneum.¹ Among common species of the fungus *M. furfur*, *M. globosa* and *M. sympodialis* are mainly involved in PV yet specifically *Malassezia furfur*, a fungus of the skin flora grow on non-affected skin.² Although many factors can get involved in the yeast proliferation, it is more common after adolescence with hormonal changes due to its correlation with sebaceous activity under influence of androgen.^{3,4} There is production of azelaic acid from the

yeast under sunlight that suppress tyrosine kinase. The process causes the hyper or hypo pigmented spots.⁵

The prevalence of Pityriasis Versicolor is in all parts of the world, in all races and in both the genders. It is usually between the age 16 to 40 years and found rarely in children and elderly.⁶ Humidity and heat triggers Pityriasis Versicolor, so its high prevalence is reported in tropical zones where humidity is higher and incidence is reported from 30 to 40 %.⁷ Evidence does not suggest Pityriasis Versicolor to be contagious. The population more susceptible to the disease is those with genetic predisposition and poor health status. Other factors include immunocompromised states like cancer, pregnancy, use of oral contraceptives and hyperhidrosis.⁸ Pityriasis

Versicolor appears at upper arms and trunk covered with brany scales however other body parts may also get effected.⁷ The disease leads the skin to discolor and does not causes any serious health risk, however, patients may have psychological as well as social stress due to it.⁹

Pityriasis Versicolor is easily diagnosed on the basis of clinical symptoms and history. Further confirmation is done using mycological examination including wood's lamp and KOH mount.¹⁰

Skin scrapings examined through microscopic evaluations, where scales after soaking with 15% KOH are appeared typically as 'spaghetti and meatball', which shows the presence of fungal hyphae. The meat balls are in fact the spores of *M. furfur* while spaghetti are the broken pseudohyphae.^{11,12} If needed it may be confirmed by taking skin biopsy where doubtful.⁴

Pityriasis Versicolor mostly remains asymptomatic, the concerns of patients are usually regarding the pigmentary changes at the areas involved and spontaneous improvement is not observed in majority of cases, therefore they seek for consultation due to cosmetic reasons. Both topical and systemic treatments are available for Pityriasis Versicolor. Topical treatments mostly suggested include Selenium Sulfide, Ketoconazole, Clotrimazole, Allylamine, Nystatin and some others. These agents are mostly suggested at new cases and can be curative in some of those but have poor compliance due to inconvenience if required to be applied at large lesions and ultimately reported as treatment failure. Similarly, low response ratio and relapses are the disadvantages.¹³⁻¹⁶

Systemic agents are the antifungal "azole" drugs that are mostly reserved and used after topical agents. These include Fluconazole, Itraconazole and Ketoconazole. The treatment aims to get rid of the fungus and must have good tolerability and safety profile. Among these ketoconazole was either restricted or banned by many health authorities including that of European Union due to the risk of hepatotoxicity, effect on adrenal metabolism and other drug interactions.¹⁷

The two agents Fluconazole and Itraconazole are now the treatment of choice among systemic agents. Itraconazole is an oral synthetic triazole while Fluconazole is an oral synthetic bis-triazole compound. These both acts by inhibiting the cytochrome-P450 dependent 14-alpha-demethylation step in the formation of ergosterol thereby impairing the functions of certain membrane bound enzyme systems, and ultimately inhibiting the growth of fungi.¹⁸

Both the drugs have been studied in different dose regimen, however, there are variable results in studies on this subject. There is still no standard drug and its dosage that can ensure complete cure.^{8,19,20,21} The topical treatment is still preferred before opting for oral treatment. Our study was therefore planned in above scenario to compare the efficacy of single dose Fluconazole (400 mg stat) vs single dose Itraconazole (1000 mg stat) in the treatment of Pityriasis Versicolor in local population of Pakistan. The results of this study will be helpful to decide the better treatment option with convenient dosage schedule in the treatment of Pityriasis Versicolor.

Methodology

This randomized control trial was conducted at the Department of Dermatology, Combined Military Hospital, Abbottabad, Pakistan, over a period of six months, from March 2022 to September 2022 after approval from Ethical Review Committee. (Ref: CMHAtD-ETH-32-Derma-22)

A total of 60 patients coming to OPD of the department and diagnosed with Tinea Versicolor were randomized in 2 equal groups of 30 patients each. Patients diagnosed on odd serial number were allocated to group A and were prescribed oral Fluconazole (400mg) while patients diagnosed on even serial number were allocated to group B and were prescribed oral Itraconazole (1000 mg stat).

All the patients above 18 years of age diagnosed with Pityriasis Versicolor were included in this study. Diagnosis was made clinically and then by using mycological tests. Clinically the disease appeared as scaly hypo/ hyperpigmented lesions, while on Woods lamps examination yellowish fluorescence was seen. Diagnosis was further confirmed with the help of KOH mount where scraping of the affected area was done with the help of glass slide and this scraping was dissolved in a solution of 10% KOH. A typical "Spaghetti and meatballs" observed under microscope confirmed the diagnosis of Pityriasis Versicolor.

Those patients who had received any antifungal treatment during last 1 month, with pregnancy or lactation, any history of renal disease, hepatic disease or malignancy were excluded.

Follow up visit was asked at completion of 2nd and 4th weeks of start of the treatment. Primary outcome was set as efficacy in treating Pityriasis Versicolor confirmed by KOH mount test at follow up visit after 4 weeks.

All the data was analyzed using SPSS version 25. The quantitative variables were calculated by taking means \pm SD. The qualitative variables were calculated by taking frequency and percentages. Chi-square test was used to compare the efficacy between two groups where p-value of ≤ 0.05 was taken as significant. A written consent was taken from the patients for the participation in study. Permission for conducting study was taken from the ethical committee of Combined Military Hospital, Abbottabad, Pakistan.

Results

The mean age in our study was 30.066 ± 7.74 years with a range of 19 to 40 years. Mean duration of symptoms was 4.216 ± 1.29 months with mean duration of 2 to 7 months.

These details for group-A and Group-B are shown in Table I. Male gender was dominant in total population, group wise details are as shown in Table II.

Table I: Mean \pm SD of patients according to age and duration of disease in both groups. (n=60)

Demographics	Group-A Mean \pm SD (n=30)	Group-B Mean \pm SD (n=30)
Age (years)	29.2 ± 7.98	30.933 ± 7.53
Duration of Symptoms (months)	4 ± 1.17	4.433 ± 1.38

Table II: Frequency and percentage of patients as per gender in both groups. (n=60)

Gender	Group-A n=30 n (%)	Group-B n=30 n (%)
Male	14 (46.66%)	18 (60%)
Female	16 (53.33%)	12 (40%)
Total	30 (100%)	30 (100%)

At the completion of two-week study period, fluconazole (400mg) was found more effective than itraconazole (1000mg) when given in single oral dose, however difference was not statistically significant as shown in Table III.

Table-III: Comparison of Efficacy in both groups after 2 weeks. (n=60)

Efficacy	After 2 weeks		P value
	Group-A (n=30)	Group-B (n=30)	
Yes	19 (63.33%)	12 (40%)	0.070
No	11 (36.66%)	18 (60%)	
Total	30 (100%)	30 (100%)	

At the completion of four-week study period, Fluconazole (400mg) was found significantly more effective than

Itraconazole (1000mg) when given in single oral doses as shown in Table IV

Table IV: Comparison of Efficacy in both groups after 4 weeks. (n=60)

Efficacy	After 4 weeks		P value
	Group-A n=30	Group-B n=30	
Yes	25 (83.33%)	17 (56.66%)	0.024
No	5 (16.66%)	13 (43.33%)	
Total	30 (100%)	30 (100%)	

There was a good tolerability in both groups without any serious adverse reactions reported.

Discussion

Topical treatments, although effectively treats Pityriasis Versicolor but there are frequent reports of recurrences hence the role of systemic treatment is very prominent in these cases.²² Fluconazole and Itraconazole are the two most extensively and successfully used systemic drugs. These drugs were given for varying periods and used with different dosage regimen in different studies. Fluconazole (300mg) in 2 doses with an interval of one week has been used effectively. Fluconazole (400 mg) as a single dose has also been used in some studies and found to cure Pityriasis Versicolor. Itraconazole 200 mg/day was given in a dose of for 7 days in some studies, however, higher concentrations of Itraconazole in the stratum corneum are achieved that persist for 3–4 weeks, the drug is presumed to be effective even in a single dose.^{23,24}

El-Reyani et al in their study published in 2018 reported that oral Fluconazole was effective in 83.3% of patients compared to 52.6% efficacy observed with oral Itraconazole in cases of Pityriasis Versicolor after the completion of 4 weeks of treatment.²⁵ In a study conducted by Ravindranath et al, clinical cure of single oral Fluconazole (400mg) and topical Clotrimazole for one month in Pityriasis versicolor was 86%.²⁰ Kausar et al in 2017 shared their results of study with oral Itraconazole (400mg) single dose in the treatment of Pityriasis Versicolor and reported 20% efficacy in 2 week time while efficacy was 60% assessed mycologically after 6 weeks.²

In a recent study conducted in Pakistani population in patients with Pityriasis Versicolor comparing the efficacy of oral Fluconazole (150mg) biweekly for 2 consecutive weeks and Itraconazole (400mg) once weekly for 2 consecutive weeks, Fluconazole was reported to be more effective than Itraconazole, assessed mycologically after a period of 4 weeks.

Siddeshwara MG and his team conducted a study for comparison of efficacy of single dose of Fluconazole (400mg) and single dose of Itraconazole (1000mg) in the treatment of Pityriasis Versicolor assessed after 2 week and then 4 week time. The results of the study showed mycological cure of 82% with Fluconazole while it was 56% with Itraconazole which was statistically significant in favor of Fluconazole after the completion of 4 weeks follow up.⁸

The results of our study are also in line with above studies carried out by Siddeshwara MG and Rizwan M with these systemic drugs for the treatment of Pityriasis Versicolor. The mean age in our study was 30.066 ± 7.74 years and was comparative between two groups. The mean duration of the disease was calculated as 4.216 ± 1.29 months and was also comparative between the two groups. Male gender was a bit dominant in overall study population (53.33%) and in group B (60%) but difference was not statistically significant. The efficacy examined mycologically through 10% KOH mount test shows a better efficacy with in Fluconazole group (63.33%) compared to Itraconazole group (40%) after 2 week times however it was not statistically significant. At the completion of study (follow up visit after 4 weeks), Fluconazole (400mg) as single dose was significantly more effective (83.33%) than Itraconazole (1000mg) as single dose (56.66%) in the treatment of Pityriasis Versicolor examined through 10% KOH mount test. Both of these oral drugs for Pityriasis Versicolor were safe with no report of side effects as also reported in previous studies with these drugs.^{8,21}

The strengths of this study was that it provided a good evidence for the association as it was a randomized controlled trial and blinding was also done.

The limitations of the study were the use of non-random convenience sampling technique and not doing the comparison of other drugs efficacious for PV infection with each other.

Conclusion

Single oral dose of Fluconazole is more effective compared to single oral dose of Itraconazole in the treatment of Pityriasis Versicolor.

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