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COMPARATIVE EFFICACY OF TOPICAL 1% CLOTRIMAZOLE VS ORAL ITRACONAZOLE IN THE TREATMENT OF PITYRIASIS VERSICOLOR

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Abstract

Objective: To compare the clinical efficacy of topical 1% clotrimazole with oral itraconazole in the treatment of pityriasis versicolor.

Study Design: Randomized controlled trial.

Place and Duration of the Study: This study was conducted in the Department of Dermatology, Combined Military Hospital (CMH), Abbottabad, from June 2025 to September 2025.

Methodology: 86 with clinically diagnosed pityriasis versicolor were enrolled and randomly assigned into two equal groups. Group A (n = 43) received topical 1% clotrimazole while Group B (n = 43) was treated with oral itraconazole. Clinical efficacy was assessed at four weeks of treatment. Quantitative variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages.

Results: The mean age of patients was 29.53 ± 3.69 years. Clinical efficacy was significantly higher in the topical clotrimazole group compared to the oral itraconazole group (93.0% vs 55.8%, $p < 0.001$). Stratified analysis proved that topical clotrimazole was much more effective in various age, gender, body mass index and moderate and severe disease cases ($p < 0.05$) in patients.

Conclusion: Topical clotrimazole 1% had better clinical effectiveness than oral itraconazole and can be regarded as an effective initial agent of pityriasis versicolor.

Keywords: Pityriasis versicolor; Clotrimazole; Itraconazole; Clinical efficacy

INTRODUCTION

Pityriasis versicolor is a common superficial fungal infection of the skin characterized by hypo- or hyperpigmented, finely scaly macules and patches that predominantly involve the upper trunk, neck and proximal upper extremities [1]. Lipophilic yeasts of the genus Malassezia that belong to the normal cutaneous flora are the cause of the condition but can become pathogenic under the right circumstances [2]. Even though it has been deemed that pityriasis versicolor is

a benign disease, its prevalence rate is high, recurrent and cosmetically disfiguring, which results in frequent dermatology visits in many parts of the globe. The extent of pityriasis versicolor differs all over the world in relation to geographical location and climatic conditions. The rate is between 1% and 4% in temperate and up to 30-40% in the tropical and subtropical regions [3]. Malassezia proliferation is most often seen in adolescents and young adults, when sebaceous glands become active and they offer a good lipid-rich growth environment [4]. Others predisposing factors are hot and humid climates, excessive sweating, occlusive clothing, immunosuppression, malnutrition and some endocrine disorders [5]. The pathogenesis of pityriasis versicolor is linked to several Malassezia species, among them, the most commonly isolated ones are Malassezia globosa, Malassezia furfur and Malassezia sympodialis [6]. The pathogenicity of these yeasts is explained by their potential to develop out of a commensal form of yeast to the pathogenic form of mycelium, which produce dicarboxylic acids and other products, which impede the functioning of melanocytes and the formation of the melanosomes, leading to pigmentary alterations [7]. Besides pigmentary changes, the patients can develop mild pruritus, scaling, which is also worsened by heat and sweat.

Although pityriasis versicolor is benign, it affects the quality of life of patients greatly, especially because of the visible color changes on the skin and regular reoccurrence [8]. The repeated nature of the treatment due to the chronic and relapsing nature of the disease means that such a treatment may be unsafe in the long term and may also compromise patient adherence and antifungal resistance. The choice of a successful and safe form of therapy is one of the main considerations in clinical practice. Treatment of pityriasis versicolor mainly aims at the reduction of the fungus load and presentation of clinical clearance. Topical and systemic antifungal agents are employed with the use of both being dependent on the severity of the disease, its spread and recurrence. Topical antifungal agents, like azoles (clotrimazole, ketoconazole, terbinafine, ciclopirox olamine and non-specific agents (selenium sulfide and zinc pyrithione) are mostly suggested as initial therapy to localized disease because of their good safety profile and poor systemic absorption [9]. These agents are mostly well tolerated and they can be used again and again which is more than enough considering the recurrent nature of the condition. Systemic antifungal agents especially itraconazole and fluconazole are normally used in cases of pityriasis versicolor that are widespread, recurrent or refractory [10]. Although systemic therapy can potentially provide a quick clinical response, it is linked to the possibility of adverse effects such as gastrointestinal intolerance, drug interactions and hepatotoxicity that restrict its routine and repeated administration. In addition, the growing concerns of antifungal resistance in superficial mycoses have placed emphasis on the need to prescribe antifungal agents rationally, especially with the systemic antifungal agents [11]

Objective

The aim of the study was to test the effectiveness of topical clotrimazole 1% versus oral itraconazole in treating pityriasis versicolor.

METHODOLOGY

This randomized controlled trial was conducted in the Department of Dermatology, Combined Military Hospital (CMH), Abbottabad, Pakistan from June 2025 to September 2025. The participants were outpatients visiting the dermatology department clinically suspected of pityriasis versicolor, who were aged 15-50 years of either gender. The diagnosis was made due to typical clinical characteristics and was confirmed by Wood lamp test and potassium hydroxide (KOH) mount of the skin scrapings collected on the active lesions. The calculation of the sample size was performed through the WHO sample size calculator using a predicted efficacy of topical clotrimazole 93.3% and oral itraconazole 70% with a confidence level of 95% and power of the study 80%. The sample size calculated was 86 patients and 43 patients on each one of the treatment groups. The treatment groups were allocated the patients through a blocked randomization method so that the groups could be equal. The study involved patients between 15-50 years of both genders with a confirmed clinical and mycological case of pityriasis versicolor. The patients were not included in case they had used topical or systemic antifungal therapy within the last one-month, systemic steroids or immunosuppressive drugs, pregnant or lactating or had diabetes mellitus, chronic systemic disease or known hepatic disease.

Data collection

The patients who had informed written consent were randomly assigned to two groups after that. Group A was treated to the topical 1% of clotrimazole twice daily during the course of two weeks and Group B was treated with oral itraconazole 200mg/kg/day in a course of five days. The patients were advised on proper medication intake and compliance was enforced in the follow up visits. The patients were assessed during the baseline, two weeks and four weeks of treatment. The same dermatology resident and consultant conducted clinical assessments at every visit to reduce the inter-observer variability. The major outcome measure was efficacy, which was the total clinical clearance of pityriasis versicolor lesions, as evidenced by no visible scales and erythema at four weeks of therapy onset. Follow-up was also supported by negative KOH mount to clinical clearance. All enrolled patients were put on a predesigned

proforma where baseline demographic and clinical variables such as age, gender, body mass index, disease duration and severity, area of residence and level of education, were recorded.

Data analysis

Statistical Package of Social Sciences version 26 was used to analyze the data. The quantitative variables (age, body mass index and disease duration) were represented by mean ± standard deviation or median with interquartile range after analysing the normality based on the Shapiro-Wilk test. Frequencies and percentages were used to display categorical variables. The Chi-square test or Fisher exact test was used as a method of comparing efficacy between the two treatment groups. To control the effect modifiers, stratification was done in terms of age, gender, body mass index and severity of the disease. The statistical significance of a p-value of ≤0.05 was taken.

RESULTS

The study involved 86 patients of clinically and mycologically verified pityriasis versicolor. Patients were randomly divided into two equal groups; 43 patients were exposed to topical 1% clotrimazole and 43 patients to oral itraconazole. The mean age of the study participants was 29.53 ± 3.69 years. The mean body mass index was 24.90 ± 1.50 kg/m² while the mean duration of pityriasis versicolor was 64.17 ± 25.20 days. Male and female patients were equally represented, with 43 (50.0%) patients in each gender group. Regarding disease severity, 11 (12.8%) patients had mild disease, 38 (44.2%) had moderate disease and 37 (43.0%) had severe pityriasis versicolor. The majority of the patients were urban residents (62.8%) and 37.2% were in the rural region. Most of them were literate (98.8%). Table I summarizes baseline demographic and clinical factors of the study population.

Table I: Baseline Demographic and Clinical Characteristics of Study Participants (n = 86)

Variable	**Total (n = 86)**
Age (years)	29.53 ± 3.69
Body Mass Index (kg/m²)	24.90 ± 1.50
Duration of Pityriasis Versicolor (days)	64.17 ± 25.20
Gender	
Male	43 (50.0%)
Female	43 (50.0%)
Severity of Pityriasis Versicolor	
Mild	11 (12.8%)
Moderate	38 (44.2%)
Severe	37 (43.0%)
Area of Residence	
Rural	32 (37.2%)
Urban	54 (62.8%)
Education Status	
Illiterate	1 (1.2%)
Literate	85 (98.8%)
Treatment Group	
Topical 1% Clotrimazole	43 (50.0%)
Oral Itraconazole	43 (50.0%)

At four weeks of follow-up, clinical efficacy was achieved in 64 (74.4%) patients overall. In the topical 1% clotrimazole group, 40 out of 43 patients (93.0%) achieved clinical clearance, whereas only 24 out of 43 patients (55.8%) in the oral itraconazole group showed clinical efficacy. Treatment failure was observed in 7.0% of patients treated with topical clotrimazole compared to 44.2% of those treated with oral itraconazole. The difference in clinical efficacy between the two treatment groups was statistically significant (Chi-square = 15.64, df = 1, $p < 0.001$). Table II shows the comparison of the clinical efficacy of the treatment groups.

Table II: Comparison of Clinical Efficacy Between Treatment Groups at 4 Weeks

Treatment Group	**Efficacy Yes n (%)**	**Efficacy No n (%)**	**χ^2 (df)**	**p-value**
Topical 1% Clotrimazole	40 (93.0)	3 (7.0)		
Oral Itraconazole	24 (55.8)	19 (44.2)	**15.64 (1)**	**<0.001**
Total	64 (74.4)	22 (25.6)		

In patients having mild pityriasis versicolor, there was complete clinical efficacy between the treatment groups and no statistical analysis could be created because of the constant results. Clinical efficacy was significantly increased in the topical clotrimazole group over the oral itraconazole group of patients with moderate disease (94.7% vs 52.6%, p = 0.003). Similarly, in patients who have severe pityriasis versicolor, topical clotrimazole proved highly effective relative to oral itraconazole (87.5% vs 52.4%, p = 0.024). Topical 1% clotrimazole was found to be more effective than oral itraconazole in both men and women in a gender-wise stratified analysis. In male patients, 90.9% of patients were treated with clotrimazole which showed clinical efficacy compared to 57% of patients treated with itraconazole (p = 0.011). Among female patients, efficacy was observed in 95.2% of the clotrimazole group compared to 54.5% of the itraconazole group (p = 0.002). Clinical efficacy of topical clotrimazole was found to be significantly greater in BMI-based stratified trials of both categories in comparison with oral itraconazole. Among patients with BMI ≤ 25 kg/m², clinical efficacy was observed in 96.2% of patients treated with clotrimazole compared to 60.0% of those treated with itraconazole (p = 0.002). Similarly, in patients with BMI > 25 kg/m², efficacy was significantly higher in the clotrimazole group compared to the itraconazole group (88.2% vs 52.2%, p = 0.016). Table III shows the stratified analysis of clinical efficacy based on effect modifiers.

Table III: Stratified Analysis of Clinical Efficacy According to Effect Modifiers

Stratification Variable	Category	Clotrimazole Yes n (%)	Itraconazole Yes n (%)	p-value
Severity of PV	Mild	8 (100.0)	3 (100.0)	—
	Moderate	18 (94.7)	10 (52.6)	**0.003**
	Severe	14 (87.5)	11 (52.4)	**0.024**
Gender	Male	20 (90.9)	12 (57.1)	**0.011**
	Female	20 (95.2)	12 (54.5)	**0.002**
Age group (years)	15–25	9 (100.0)	3 (100.0)	—
	26–35	30 (90.9)	21 (52.5)	**<0.001**
	36–50	1 (100.0)	—	—
BMI (kg/m²)	≤25	25 (96.2)	12 (60.0)	**0.002**

DISCUSSION

The research was aimed to evaluate the effectiveness of topical 1% clotrimazole versus oral itraconazole in the management of pityriasis versicolor with the objective of finding an effective and safer therapeutic agent to be used in daily clinical practice. The results of this randomised controlled trial showed that topical 1% clotrimazole recorded a significantly greater clinical efficacy when compared to oral itraconazole at a four weeks follow-up. Clinical clearance was seen in 93.0% of patients who received topical clotrimazole and 55.8% receiving oral itraconazole and the difference was statistically significant (p < 0.001). Pityriasis versicolor is an ordinary superficial fungal infection especially, in tropical and subtropical areas where conditions in the environment are favorable to the growth of Malassezia species [1-3]. Even though the disease is harmless, the recurrent nature and the cosmetic effects require effective treatment measures that can be safely repeated. Recent management principles suggest the use of topical antifungal treatment of localized disease with the use of systemic antifungals as a last line of treatment of extensive or recurrent infections [12-14].

The increased activity of topical clotrimazole could be explained by the direct effect on the area of infection that results in the high local concentration of the drug with low systemic effects [15]. Oral itraconazole, as a broad-spectrum antifungal agent, requires systemic absorption, liver metabolism and patient adherence, which can all affect the outcome of the treatment [16]. The repeated use of systemic antifungals is restricted by the concerns about drug interaction and hepatotoxicity because the condition is characterized by frequent relapses [17]. The main findings were also supported by the use of severity-wise stratified analysis in the current study. Although the treatment modalities were equally effective in clearing the clinical situation of patients with mild disease, the topical clotrimazole was found to be a much more effective treatment of patients with moderate and severe pityriasis versicolor. In moderate disease, clotrimazole group had 94.7% efficacy versus itraconazole group 52.6% (p = 0.003) and moderate disease had 87.5% versus itraconazole 52.4% (p = 0.024). The above results support the notion that even in the more widespread disease topical clotrimazole may be used and that the view that systemic treatment is always needed in moderate and severe cases is not always correct. Stratified analyses in terms of gender and age showed that the topical clotrimazole was more superior than both male and female patients as well as various age groups. Topical clotrimazole was much more effective than oral itraconazole in the age group of 26-35 years (the major part of the population of the study) 90.9% vs 52.5% (p < 0.001). Increased efficacy of clotrimazole in both types of BMI was found showing

that body mass index did not change the effect of treatment. These results highlight the effectiveness of topical therapy in various subpopulations of patients. The findings of this research work are in line with the already existing local and international literature. The cure rate was significantly higher with topical clotrimazole than with oral itraconazole (93.3% vs 70%), which is very similar to that in the case of the current study [18]. The use of topical azoles in the treatment of pityriasis versicolor has also attracted attention of other studies together with systematic reviews that have posited that this agent is effective in reducing the recurrence and the number of adverse effects [10-12]. There is emerging evidence of antifungal resistance and futility of treatment using systemic antifungal hence the need to choose antifungals rationally [19,20]. The clinical benefit of safe, effective and easily available topical agent like clotrimazole, given the recurring nature of pityriasis versicolor, is apparent. The study was done in one center and follow-up was rather short and no further evaluation of long-term recurrence rates was done. Also, mycological cure was not assessed in all patients in a follow-up, which can be a limitation to assess full fungal clearance.

CONCLUSION

Topical 1% clotrimazole demonstrated significantly higher clinical efficacy than oral itraconazole in the treatment of pityriasis versicolor. The results indicate that topical clotrimazole should be used as the first line treatment to treat various groups of patients, which is more likely to yield better results and is less likely to be associated with side effects like systemic antifungal therapy.

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