



Original Article



Exploring the Efficacy of Ketoconazole versus Ketoconazole Combined with Adapalene in Treating Pityriasis Versicolor: A Comparative Study

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ABSTRACT

Pityriasis versicolor, a fungal infection causing skin discoloration, was commonly treated with antifungal agents like ketoconazole and adapalene, either alone or in combination. **Objective:** To compare the efficacy of ketoconazole alone versus the combination of ketoconazole and adapalene in the treatment of pityriasis versicolor. **Methods:** This study was conducted at Department of Pharmacology, Bannu Medical College, Bannu from May 2023 to October 2023. Total 90 (45 in each group) adult patients diagnosed with the condition were assigned to either treatment group. Group A was treated with ketoconazole 2% cream monotherapy, while Group-B was given combined therapy with ketoconazole 2% cream and adapalene 1% gel. Both groups underwent treatment for duration of four weeks, with instructions for application provided by the investigators. Treatment outcomes, including lesion clearance rates were evaluated at follow-up. The collected data underwent processing and analysis utilizing IBM SPSS, version 23.0. **Results:** Out of total participants 57(63.3%) were male and 33(36.7%) were females, with a mean age of 30.63 ± 8.38 years. Regarding lesion type, the distribution between hyperpigmented (51.1%) and hypopigmented (48.9%) lesions were relatively balanced. This study depicted a significantly higher proportion of patients in the combination therapy group ($n=39, 86.7\%$) experienced improvement compared to those in the ketoconazole monotherapy group 21 (46.7%) ($p < 0.001$). **Conclusions:** In conclusion, this study demonstrates that the combination of ketoconazole and adapalene exhibits superior efficacy compared to ketoconazole alone in treating pityriasis versicolor.

INTRODUCTION

Pityriasis versicolor, often known as "tinea versicolor," is a prevalent fungal skin disease. Although this condition can be a rather harmless one, the skin's signature appearance of discolored patches is often displeasing and leads to embarrassment in the patients affected by the condition [1, 2]. Therefore, to enhance understanding of pityriasis versicolor by both the healthcare providers and the patients, the causes, morphology, diagnosis, and available treatment options for this condition should be well understood [3]. The cause of this is the yeast *malassezia furfur*, which is present on everyone's skin inherently [4, 5]. Pityriasis versicolor can occur if this yeast multiplies under certain conditions mainly when there is warm and humid

conditions or excessive secretion of sebum. Small round or oval macules are some of the most common complaints in pityriasis versicolor. These patches differ in colour as of brown, white, tan or pink depending on the colour of the skin of the patients. In persons, they manifest more on areas that are normally profusely sweating, including the chest, back, shoulders, and upper arms. Occasionally, the affect area of skin may be associated with modest itching or slight dryness of the skin [6]. Physician usually diagnose pityriasis versicolor usually through visual examination of skin by naked eyes. Sometimes reveals additional information is revealed from skin scrapings or Wood's lamp examination for typical mycological features. They found



out that pityriasis versicolor must be differentiated from other diseases that exhibit similar symptoms, for example, vitiligo, or eczema to give it the right treatment [7]. A number of therapeutic strategies are generally prescribed for pityriasis versicolor and these include the use of anti-fungal agents, which can be applied in form of creams, lotions or shampoos. These medications help to get rid of the yeast and allow the normal processes of self-cleaning of the skin flora. A type of systemic antifungal drug commonly employed is ketoconazole, which is well researched in the treatment of pityriasis versicolor [8]. When administered alone ketoconazole exerts its action through suppressing the growth of the aetiologic agent, which is *Malassezia furfur*. It also comes in the form of creams, shampoos, and oral tablets to suite the extent and areas of infection [9]. Over the last few years, there have been interest towards combination therapy of ketoconazole with adapalene to improve the prognosis of pityriasis versicolor. Adapalene is an anti-inflammatory substance that also contains properties of a keratolytic agent, thus making it compatible with ketoconazole in this regard. Pityriasis versicolor is thus treated by both the fungicidal effect reducing the fungal overgrowth, and the inflammatory and skin turnover effect, trying to manage all the areas affected [10].

The purpose of this study was to establish whether the combination of ketoconazole with adapalene has more effective in the treatment of pityriasis versicolor. In seeking to study this potentially complementary combination therapy, it was aimed to treat both the antifungal and inflammation triggers of the disease to perhaps improve the treatment results. This research could prove to be very useful in expanding the understanding of how to better deal with pityriasis versicolor; thus, providing a broader approach to treat this frequently encountered fungal disorder. Furthermore, the assessment of the efficacy of this combination therapy would help to cover the reported lack of relevant literatures, and contribute to the derationing of evidence-based management of pityriasis versicolor for clinicians.

METHODS

The study was done after getting ethical clearance from the set institutional review body (BMC/IRB/23/37). This study was conducted in the department of pharmacology, Banu Medical College, Banu from May to the end of October in the year 2023. Type of study adopted was experimental study. This research conformed to World Medical Association Declaration of Helsinki, and participants' written informed consent secured beforehand; patient-identifying information was kept confidential and anonymous. A prospective, randomized comparative study design was used. The sample size was determined using

WHO calculator (www.openepi.com) assuming improvement with the combination therapy ketoconazole 2% cream and adapalene 1% gel to be (87.5%) compared to ketoconazole alone (47.5%) with a power of 80% and a significance level of 0.05 using a two-sample proportion formula for independent samples [11]. Pityriasis versicolor was identified clinically and verified by microbiological microscopy or culture in adult individuals. Excluded patients had allergies to study drugs or dermatological disorders. Participants were assigned to two treatment groups: Group A was treated with Ketoconazole 2% cream monotherapy, while Group-B was given combined therapy with ketoconazole 2% cream and adapalene 1% gel. Both groups underwent treatment for duration of four weeks, with instructions for application provided by the investigators. Treatment commenced promptly upon diagnosis and continued for 4 weeks. Follow-up assessments were scheduled at 1-month intervals post-treatment initiation to monitor progress and evaluate treatment outcomes. The primary outcome measure was the percentage of participants achieving complete clearance of pityriasis versicolor lesions. Complete clearance of Pityriasis versicolor lesions was defined as the absence of visible lesions upon clinical examination and confirmed by photographic documentation at the end of the treatment period. Specifically, lesions were considered cleared if no signs of scaling, erythema, or hypopigmentation were observed. Clinical evaluation of skin lesions was performed using wood's light lamp by trained dermatologists. The infected areas typically exhibit a yellow-green fluorescence under wood's light [22]. Compliance was monitored through regular follow-ups, and any mild irritation or redness at the application site was documented as an adverse effect. The assessment of adverse effect mild irritation was labeled as slight discomfort or redness at the application site, noticeable but not interfering significantly with daily activities or requiring specific treatment. Satisfaction levels were categorized into "well satisfied" for strong positive feedback, "moderately satisfied" for mixed responses, and "unsatisfied" for negative feedback, based on patient self-reports. The data were analyzed using the statistical software SPSS version 23.0. The mean and standard deviation were employed to analyzed quantitative data such as age and duration of disease. Qualitative factors (gender, type of lesion, improvement yes/no, side effects yes/no, patients satisfaction) were analyzed to determine their frequency and percentage. Chi-square tests and unpaired t-test were employed to assess the comparative effectiveness of the treatments in the two groups. A p-value less than 0.05 was considered to be statistically significant.

RESULTS

The baseline characteristics of the participants were

summarized in table 1. Many participants i.e. 57 (63.3%) were male, with an average age of 30.63 ± 8.38 years. Most patients fell within the age group of 18-30 years 58 (64.4%), and the duration of the disease varied, with a substantial proportion 31 (34.4%) experiencing symptoms for 1-2 months. Regarding lesion type, the distribution between hyperpigmented (51.1%) and hypopigmented (48.9%) lesions was relatively balanced.

Table 1: Baseline Characteristics of Study Participants

Variables	N (%) / Mean \pm SD
Gender	
Female	33 (36.7)
Male	57 (63.3)
Age Groups (Years)	
18-30	58 (64.4)
31-50	32 (35.6)
Age (Years)	30.63 \pm 8.38
Less than 1 Month	30 (33.3)
1-2 Months	31 (34.4)
More than 2 Months	29 (32.2)
Type of Lesion	
Hyperpigmented	46 (51.1)
Hypopigmented	44 (48.9)

Table 2 presented a comparison between the two treatment groups concerning baseline characteristics. No statistically significant differences were observed between the groups in terms of gender, age distribution, age mean, duration of disease, or type of lesion.

Table 2: Comparison between the Treatment Groups Regarding Baseline Data

Variables	Group A	Group B	p-Value
	N (%) / Mean \pm SD	N (%) / Mean \pm SD	
Gender			
Female	16 (35.6)	17 (37.8)	0.827 ^a
Male	29 (64.4)	28 (62.2)	
Age Groups (Years)			
18-30	28 (62.2)	30 (66.7)	0.660 ^a
31-50	17 (37.8)	15 (33.3)	
Age (Years)	31.4 \pm 8.46	29.9 \pm 8.32	0.402 ^b
Duration of Disease			
<1 month	16 (35.6)	14 (31.1)	0.905 ^a
1-2 month	15 (33.3)	16 (35.6)	
>2 month	14 (31.1)	15 (33.3)	
Type of Lesion			
Hyperpigmented	21 (46.7)	25 (55.6)	0.399 ^a
Hypopigmented	24 (53.3)	20 (44.4)	

^aChi square test; ^bUnpaired t-test

The efficacy of the treatment regimens was evaluated based on the improvement observed in the patients. As depicted in Table 3, a significantly higher proportion of patients in the combination therapy group (n=39, 86.7%) showed improvement compared to those in the Ketoconazole monotherapy group 21(46.7%)($p < 0.001$).

Table 3: Comparison of Improvement between Treatment Groups

Improvement	Group A	Group B	p-value
	N (%)	N (%)	
Yes	21 (46.7)	39 (86.7)	< 0.001 ^a
No	24 (53.3)	6 (13.3)	

^aChi square test

Regarding side effects and patients' satisfaction, the combination therapy group reported a higher incidence of mild irritation (n= 16, 35.6%) compared to the Ketoconazole monotherapy group (n=3, 6.7%) ($p < 0.001$). However, patients in the combination therapy group also exhibited higher satisfaction levels, with 55.6% reporting being well satisfied, compared to 31.1% in the monotherapy group ($p = 0.048$)(Table 4).

Table 4: Comparison between the Treatment Groups Regarding Side Effects and Patients' Satisfaction

Treatment	Group A	Group B	p-Value ^a
	N (%)	N (%)	
Side Effects (Mild Irritation)	3 (6.7)	16 (35.6)	<0.001
Patients Satisfaction			
Well Satisfied	14 (31.1)	25 (55.6)	0.04
Moderately Satisfied	20 (44.4)	15 (33.3)	
Unsatisfied	11 (24.4)	5 (11.1)	

^aChi square test

DISCUSSION

Pityriasis versicolor, a common fungal infection of the skin, presents with characteristic discolored patches that can cause discomfort and self-consciousness. Ketoconazole, a widely used antifungal medication, has been a mainstay in the treatment of this condition, effectively targeting the underlying fungal overgrowth. Nonetheless, new studies show that ketoconazole increases adapalene, an anti-inflammatory compound, leading to better results in sufferers of pityriasis versicolor. Thus, the purpose of this work was to compare the effectiveness of ketoconazole used alone and in combination with adapalene, which will help in determining the further approach to the treatment of this dermatological lesion [12, 13]. Similar to Jha S findings, this study observed a higher prevalence of males, with 63.3% males and 36.7% females. Participants mean age 30.63 (SD =8. 38) was quite comparable to Jha S in participant's age of 31.1 (SD =9. 22) Likewise, participant's age distribution especially in younger age group of 18 to 30 years confirm both this study finding and that of Jha S [14]. Additionally, while this study noted variability in the duration of the disease, ranging from one to two months in a substantial proportion of patients (34. 4%), Mohankar's findings corroborate the notion of a relatively short duration of symptoms, with an average duration of three months (range: (First time users - 1 to 6 months) [15]. The outcomes of this study corroborate the research of Hameed S et al., in 2022, namely, the higher efficacy of combination therapy as opposed to monotherapy for pityriasis versicolor. In the present study, a significantly

higher proportion of patients in the combination therapy group 39 (86.7%) showed improvement compared to those in the ketoconazole monotherapy group 21 (46.7%) ($p < 0.001$) [16]. The present study established the results same as Tawfik KM *et al.*, in 2022 who established that in the frequency of improvement, a combination of drugs fared much better than Ketoconazole [17]. Shi TW *et al.*, in 2015 conducted the study on the effectiveness of different concentrations of adapalene in treating acne and established that combined therapy with ketoconazole 2% cream and adapalene 1% gel has been shown to increase the ratio of the patients who felt improvement compared to the control group (92% vs 72%; $P= 0.0009$), which was in parallel to this findings [18, 19]. Further, the findings of this research were in harmony and line with other research carried out by Gobbato AA *et al.*, in 2015. The results of the present study were in line with those of Bakr E *et al.*, in 2020, who found that 93.3% of patients in the combination group and 83.3% in the monotherapy group both showed substantial improvement; this sample size was similar to that of the former [20, 21]. Results of present study were consistent with the results of other studies thus strongly support the conclusion that combining medications was more effective than using a single therapy for treating pityriasis versicolor [19-22]. Lack of long-term follow-up limits assessment of treatment durability. Future research should consider larger sample sizes and longer-term follow-up to evaluate treatment sustainability and relapse occurrence.

CONCLUSIONS

In conclusion, this study demonstrates that the combination of ketoconazole and adapalene exhibits superior efficacy compared to ketoconazole alone in treating pityriasis versicolor, highlighting the potential of combination therapy as a preferred treatment approach for this dermatological condition. These findings contribute to the optimization of therapeutic strategies, ultimately improving patient outcomes and quality of life.

Authors Contribution

Conceptualization: SH, SA

Methodology: SH, SZ, GS, SA

Formal analysis: AM, SF

Writing, review and editing: SZ, GS, SA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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