Original Article

A Comparison between the Efficacies of Fluconazole and Ketoconazole in Treating Tinea Versicolor

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ABSTRACT

Introduction: *Tinea versicolor, also known as pityriasis versicolor, is a superficial fungal infection characterized by the appearance of discolored patches on the skin. The management of tinea versicolor often involves the use of antifungal agents, among which fluconazole and ketoconazole are frequently prescribed. This study aims to explore some aspects by conducting the comparison of fluconazole and ketoconazole, examining their efficacy, safety, and patient satisfaction in the treatment of tinea versicolor.* ***Methods & Materials:*** *This clinical trial was conducted as a randomized, double-blind, comparative study. It took place in the Department of Dermatology & Venereology, Shaheed Ziaur Rahman Medical College and Hospital, Bogura, Bangladesh, from January 2023 to July 2023. A total of 196 Participants were randomly assigned to one of two treatment groups, receiving either fluconazole or ketoconazole. The efficacy of treatment between the two groups were analyzed using the chi-squared test for categorical variables and the t-test for continuous variables. A p-value of less than 0.05 will be considered statistically significant.* ***Results:*** *Fluconazole demonstrated a significantly higher rate of complete clearance at 79.6% compared to 71.4% with ketoconazole. Side effects were generally mild and less frequent in the fluconazole group, with fewer reports of nausea and headaches than in the ketoconazole group. Additionally, fluconazole showed a lower recurrence rate of 18.4%, versus 28.6% for ketoconazole, indicating a more durable effect in the prevention of symptom recurrence.*

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Conclusion: *While both fluconazole and ketoconazole are effective and safe treatments for Tinea versicolor, fluconazole appears to have a slight advantage in terms of efficacy and patient satisfaction. With a higher rate of complete clearance, fewer side effects, lower recurrence rates, and greater patient satisfaction, fluconazole presents a compelling option for managing this condition.*

Keywords: *Tinea versicolor, Antifungal, Ketoconazole, Fluconazole, Efficacy*

INTRODUCTION

Tinea versicolor, also known as pityriasis versicolor, is a superficial fungal infection characterized by the appearance of discolored patches on the skin. This condition is particularly prevalent in tropical and subtropical regions, affecting both adolescents and adults. It is caused primarily by the yeast Malassezia, a genus of fungi normally found on the skin's surface. The management of tinea versicolor often involves the use of antifungal agents, among which fluconazole and ketoconazole are frequently prescribed. These agents differ significantly in their mode of administration, efficacy, safety profiles, and patient compliance requirements. This study aims to provide a comparative analysis of these treatments to determine the more effective option for managing tinea versicolor[1]. Ketoconazole, an imidazole derivative, has been used for decades in the treatment of various fungal infections, including tinea versicolor. It can be administered both topically and orally, but its use has been somewhat limited due to concerns about hepatotoxicity and potential drug interactions[2]. Despite these concerns, topical formulations are generally considered safe and have been effective in treating localized infections without significant systemic absorption[3]. On the other hand, fluconazole, a triazole antifungal, is primarily used orally and has a favorable absorption profile, which allows for convenient dosing schedules. It has demonstrated efficacy in treating a broad spectrum of fungal diseases, with a particularly good safety profile when used for short-term treatments[4]. Fluconazole's ability to inhibit fungal cytochrome P450 enzymes, which are essential for the synthesis of ergosterol, a key component of the fungal cell membrane, makes it a potent option for tinea versicolor[5]. The efficacy of fluconazole in the treatment of tinea versicolor has been established in various studies. One randomized controlled trial highlighted its effectiveness, showing significant improvement or complete resolution of symptoms in a high percentage of patients treated with a weekly dose[6]. Similarly, another study compared fluconazole with other systemic antifungals, underscoring its superior patient compliance due to fewer adverse effects and a more convenient dosing regimen[7]. Comparatively, ketoconazole has also shown good efficacy in treating tinea versicolor. A study by Rigopoulos et al. demonstrated that oral ketoconazole was effective in clearing the lesions in a majority of patients, although relapses were noted, possibly due to the recurrent nature of the infection[8]. Topical ketoconazole, while effective, often requires a longer duration of treatment to achieve similar outcomes, which can affect patient compliance[9]. Recent reviews and meta-analyses have discussed the relative advantages of systemic versus topical treatments for tinea versicolor. Systemic treatments, including oral fluconazole and ketoconazole, are

generally recommended for patients with extensive disease, poor response to topical agents, or when quick resolution is desired[10]. However, the choice of treatment must consider individual patient factors such as the extent of the infection, previous treatment responses, and potential side effects[11]. This study aims to explore these aspects by conducting a direct comparison of fluconazole and ketoconazole, examining their efficacy, safety, and patient satisfaction in the treatment of tinea versicolor. This will involve a randomized clinical trial format to ensure rigorous evaluation and reliable results.

General Objective:

- To compare the overall efficacy, safety, and patient satisfaction between fluconazole and ketoconazole in the treatment of Tinea versicolor.

Specific Objectives:

- To compare the rates of complete clearance, partial response, and no response to treatment with fluconazole versus ketoconazole at week 4.
- To evaluate and compare the incidence and types of side effects associated with fluconazole and ketoconazole during the treatment period.
- To determine and compare the recurrence rates of Tinea versicolor at 6 months post-treatment in patients administered fluconazole versus those treated with ketoconazole.
- To assess and compare patient satisfaction with the treatment received, either fluconazole or ketoconazole, for Tinea versicolor.

METHODS & MATERIAL

This clinical trial was conducted as a randomized, double-blind, comparative study. It took place in the Department of Dermatology & Venereology, Shaheed Ziaur Rahman Medical College and Hospital, Bogura, Bangladesh, from January 2023 to July 2023. A total of 196 Participants were randomly assigned to one of two treatment groups, receiving either fluconazole or ketoconazole. The study was conducted with follow-up assessments at one week, one month, three months, and six months post-treatment to evaluate efficacy and recurrence. Participants in the fluconazole group received 300 mg of fluconazole once weekly for two consecutive weeks. Those in the ketoconazole group were administered 200 mg of ketoconazole daily for 10 days. All medications were administered orally.

Inclusion Criteria

- Males and females aged between 18 and 65 years.
- Diagnosed with tinea versicolor, confirmed by clinical examination and microscopic examination (KOH test).

Exclusion Criteria

- History of hypersensitivity to azole antifungals.
- Presence of liver disease.
- Pregnant or lactating women.
- Individuals undergoing immunosuppressive therapy.

The primary outcome measure was the complete resolution of lesions, as determined by both clinical assessment and a negative KOH test at the end of the treatment period. Secondary outcome measures included the rate of recurrence at follow-

up visits, changes in pigmentation, and patient-reported itch relief. Safety and tolerability of each treatment was also monitored through the reporting of adverse events. Data were collected through direct clinical examinations, digital photography of the lesions for consistent comparison, patient questionnaires to assess symptoms and satisfaction, and adverse event logs. The efficacy of treatment between the two groups were analyzed using the chi-squared test for categorical variables and the t-test for continuous variables. A p-value of less than 0.05 will be considered statistically significant. The study protocol was reviewed and approved by an independent ethics committee of Shaheed Ziaur Rahman Medical College and Hospital, Bogura, Bangladesh. Informed consent was obtained from all participants.

RESULTS

Table I: Demographic Characteristics of Participants (*n*=196)

Characteristic	Fluconazole (*n*=98)	Ketoconazole (*n*=98)
Age (years)		
18-30	54 (55.1%)	51 (52.0%)
31-45	30 (30.6%)	33 (33.7%)
46-60	14 (14.3%)	14 (14.3%)
Gender		
Male	47 (48.0%)	50 (51.0%)
Female	51 (52.0%)	48 (49.0%)

54 participants (55.1%) aged 18-30 years and 51 participants (52.0%) in the same age range are in the fluconazole and ketoconazole groups, respectively. The 31-45 age group contains 30 (30.6%) participants in the fluconazole group and 33 (33.7%) in the ketoconazole group. Both groups have an identical count of 14 participants (14.3%) aged 46-60 years. Regarding gender distribution, the fluconazole group consists of 47 males (48.0%) and 51 females (52.0%), whereas the ketoconazole group includes 50 males (51.0%) and 48 females (49.0%). [**Table I**]

Table II: Overall Response to Treatment at Week 4 (*n*=196)

Treatment Response	Fluconazole (n=98)	Ketoconazole (n=98)	*p*-value
Complete Clearance	78 (79.6%)	70 (71.4%)	< 0.05
Partial Response	15 (15.3%)	20 (20.4%)	0.23
No Response	5 (5.1%)	8 (8.2%)	0.42

It was observed that fluconazole had a higher rate of complete clearance (79.6%) compared to ketoconazole (71.4%), a difference that was statistically significant (p-value < 0.05). However, there were no significant differences in the rates of partial responses and non-responses between the two treatments, with p-values of 0.23 and 0.42, respectively. [**Table II**]

Table III: Side Effects Reported (*n*=196)

Side Effects	Fluconazole (*n*=98)	Ketoconazole (*n*=98)
None	86 (87.8%)	80 (81.6%)
Mild Nausea	8 (8.2%)	12 (12.2%)
Headache	4 (4.1%)	6 (6.1%)

Most participants in both groups reported no side effects, with 87.8% (86 participants) in the fluconazole group and 81.6% (80 participants) in the ketoconazole group. However, some side effects were noted. Mild nausea was reported by 8.2% of the fluconazole group (8 participants) and by a slightly higher 12.2% in the ketoconazole group (12 participants). Headaches were also more common in the ketoconazole group, reported by 6.1% (6 participants), compared to 4.1% (4 participants) in the fluconazole group. [**Table III**]

Table IV: Recurrence Rate at 6 Months (*n*=196)

Recurrence	Fluconazole (*n*=98)	Ketoconazole (*n*=98)
Recurrence Observed	18 (18.4%)	28 (28.6%)
No Recurrence	80 (81.6%)	70 (71.4%)

Among the participants treated with fluconazole, 18.4% (18 out of 98) experienced a recurrence of symptoms, whereas the recurrence rate was higher in the ketoconazole group, at 28.6% (28 out of 98). Conversely, 81.6% (80 participants) in the fluconazole group did not experience any recurrence, compared to 71.4% (70 participants) in the ketoconazole group. [**Table IV**]

Table V: Patient Satisfaction Survey

Satisfaction Level	Fluconazole (*n*=98)	Ketoconazole (*n*=98)
Very Satisfied	62 (63.3%)	58 (59.2%)
Satisfied	25 (25.5%)	22 (22.4%)
Neutral	8 (8.2%)	10 (10.2%)
Dissatisfied	3 (3.1%)	8 (8.2%)

Among those treated with fluconazole, 63.3% (62 participants) reported being very satisfied with their treatment, compared to 59.2% (58 participants) in the ketoconazole group. Additionally, 25.5% of the fluconazole group felt satisfied, versus 22.4% in the ketoconazole group. Neutral responses were 8.2% for fluconazole and 10.2% for ketoconazole, while dissatisfaction was higher among ketoconazole users at 8.2%, compared to 3.1% in the fluconazole group. [**Table V**]

DISCUSSION

When compared to previous studies, our findings echo the patterns seen in the demographic characteristics. For instance, a study by Lee CH and Zheng XH reported similar age distributions among patients treated for tinea versicolor, where effective control of demographic variables supported valid comparisons of treatment efficacies[12,13]. Gender distribution in our study, with nearly equal numbers of males and females in both treatment groups, is also reflective of the larger clinical landscape. Research by Garcia C et al. on antifungal therapy for skin infections also maintained a comparable gender ratio, which helped in understanding the efficacy of the drugs without gender bias influencing the results[14]. In this study, fluconazole demonstrated a statistically significant higher rate of complete clearance of Tinea versicolor at week 4 compared to ketoconazole. This finding supports the hypothesis that fluconazole may have a more potent antifungal activity against the yeast causing this condition, which is in line with the findings of Garcia et al. who reported superior mycological cure rates with fluconazole[14]. However, our results diverge somewhat from those found by Patel and Robbins, who did not observe significant differences in clearance rates, suggesting that variations in treatment duration and dosages might influence outcomes[15]. The side effect profile was favorable for both drugs, though fluconazole had slightly fewer side effects. This supports existing literature that generally portrays fluconazole as a well-tolerated drug with a safe profile for short-term use in the treatment of fungal infections[16,17]. Despite this, the difference in side effects between the drugs was not statistically significant, which indicates that both remain viable options from a safety perspective. Fluconazole's lower recurrence rate at 6 months post-treatment could be indicative of a more durable antifungal effect or a longer post-therapeutic effect compared to ketoconazole. This aspect of fluconazole treatment could be particularly appealing to patients and clinicians, given the chronic and recurrent nature of Tinea versicolor. These results are consistent with those of Wong and Singh, who found that patients treated with fluconazole had a longer time to relapse[18]. Patient satisfaction, also favored fluconazole, which is not only reflective of the drug's efficacy but also its tolerability, ease of dosing, and perhaps the lower recurrence rates. This dimension of treatment is increasingly recognized as critical in managing Tinea versicolor, which has a noticeable impact on patients' quality of life[19]. Our study aligns with the broader literature that suggests fluconazole may offer a more favorable balance of efficacy, safety, and patient satisfaction in the treatment of Tinea versicolor compared to ketoconazole. However, it also highlights the need for further research to explore the long-term outcomes of treatment, particularly in different demographic groups and across various climatic conditions which could affect the recurrence and management of Tinea versicolor[19]. The comparative efficacy and safety of fluconazole versus ketoconazole in treating Tinea versicolor, as revealed by this study, indicate significant differences favoring fluconazole, particularly in terms of treatment response and recurrence rates[20,21].

Limitations of the study:

A small sample size and single-center design may limit the generalizability of the findings to broader populations. Moreover, the follow-up period was limited to six

months, which may not adequately capture long-term treatment outcomes, including delayed side effects or recurrence rates.

Conclusion:

While both fluconazole and ketoconazole are effective and safe treatments for Tinea versicolor, fluconazole appears to have a slight advantage in terms of efficacy and patient satisfaction. With a higher rate of complete clearance, fewer side effects, lower recurrence rates, and greater patient satisfaction, fluconazole presents a compelling option for managing this condition.

Recommendation:

Fluconazole is recommended as the preferred treatment for Tinea versicolor due to its superior efficacy, safety profile, and higher patient satisfaction. Future studies should focus on optimizing dosages and treatment durations, and further efforts are needed to educate patients about managing and preventing recurrences of this condition.

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