Original Article

Effects of Itraconazole in Tinea Corporis in All Age Group

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ABSTRACT

Introduction*: Tinea corporis, commonly known as ringworm, is a superficial fungal infection predominantly affecting the glabrous (smooth and bare) skin apart from the scalp, feet, and groin. Current research continues to explore the scope of itraconazole's utility in tinea corporis, with studies focusing on optimizing dosing regimens and minimizing side effects in different age groups.* ***Methods & materials:*** *This study employed a cross-sectional prospective design to assess the effectiveness and safety of itraconazole in treating Tinea corporis across different age groups, in the Department of Dermatology, Mymensingh Medical College and Hospital, Mymensingh, Bangladesh, from July 2023 to January 2024. A total of 472 patients were selected for his study. Data were analyzed using SPSS and significance was set at p<0.05.* ***Results****: Initial findings at the two-week follow-up indicated that 58-67% of participants across age groups experienced complete clearing of lesions, with additional significant improvements noted. By the four-week follow-up, the rates of complete clearing had increased: 82% in children (2-12 years), 86% in adolescents and young adults (13-35 years), 89% in middle-aged adults (36-60 years), and 88% in the elderly (>60 years). Despite these high rates of efficacy, statistical analysis determined that there were no significant differences between age groups (p > 0.05).* ***Conclusion:*** *The study demonstrates that itraconazole effectively treats Tinea Corporis across various age groups with consistent efficacy. The results show significant lesion clearance and symptom resolution within four weeks, with no notable differences in response across age demographics.*

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INTRODUCTION

Tinea corporis, commonly known as ringworm, is a superficial fungal infection predominantly affecting the glabrous (smooth and bare) skin apart from the scalp, feet, and groin. The causative agents are dermatophytes, mainly species from the genera Trichophyton, Microsporum, and Epidermophyton[1]. Characterized by round or oval erythematous, scaly plaques that may be itchy and sometimes ring-like, tinea corporis poses a global health concern due to its potential for rapid spread and significant discomfort. Although common in all age groups, its prevalence and presentation can vary significantly, influencing treatment approaches and outcomes. Itraconazole, a triazole antifungal agent, has been extensively used in the treatment of various fungal infections, including tinea corporis[2]. Its mechanism of action involves inhibiting the fungal cytochrome P450 enzyme, which is essential for the synthesis of ergosterol, a vital component of fungal cell membranes[3]. The disruption of ergosterol synthesis leads to increased cellular permeability and ultimately the death of the fungal cell. Given its efficacy against a broad spectrum of fungi and favorable pharmacokinetic properties, itraconazole has emerged as a preferred option for the treatment of dermatophytoses not only in adults but also in pediatric populations[4]. The significance of itraconazole in the treatment of tinea corporis across all age groups cannot be understated. This drug offers several advantages, including good oral bioavailability, a broad antifungal spectrum, and a relatively safe profile with minimal adverse effects compared to other systemic antifungals[5]. Moreover, itraconazole's ability to accumulate in keratin-rich tissues like the skin provides effective and sustained antifungal activity, which is crucial for treating tinea corporis[6]. The effectiveness of itraconazole in various dosing schedules, ranging from continuous to pulse dosing, facilitates flexibility in managing tinea corporis, and adapting to patient-specific needs and compliance levels[7]. Clinical studies have demonstrated itraconazole's efficacy in treating tinea corporis with varying dosages and durations tailored to the severity of the infection and patient characteristics, including age. For instance, pulse dosing regimes have shown high efficacy and tolerability in both pediatric and elderly populations, addressing concerns regarding systemic exposure and potential toxicity[8]. In comparative studies, itraconazole has often shown superior or comparable efficacy to other antifungal agents like terbinafine and fluconazole, with the added benefit of a shorter duration of treatment in some cases[9]. However, while itraconazole is generally well-tolerated, its use is not devoid of challenges. The potential for drug-drug interactions and side effects, particularly cardiotoxicity, hepatotoxicity, necessitates careful consideration, especially in patients with pre-existing liver conditions or those taking other medications metabolized via the cytochrome P450 pathway[10]. These considerations are particularly pertinent in the elderly, who are more likely to have comorbid conditions and polypharmacy. In children, dosing adjustments and monitoring are crucial due to the variable pharmacokinetics in this population[11]. Current research continues to explore the scope of itraconazole's utility in tinea corporis, with

studies focusing on optimizing dosing regimens, minimizing side effects, and overcoming challenges such as resistance. Resistance to antifungal agents, though less common in dermatophytes compared to other fungi, is an evolving concern that underscores the need for ongoing surveillance and development of novel therapeutic strategies[12].

OBJECTIVES

General Objective:

To evaluate the efficacy of itraconazole in treating Tinea Corporis across different age groups.

Specific Objectives:

- To determine the rate of lesion clearing in patients treated with itraconazole over four weeks.
- To compare the efficacy of itraconazole treatment across four age groups: children (2-12 years), adolescents and young adults (13-35 years), middle-aged adults (36-60 years), and the elderly (over 60 years).
- To assess the symptom resolution at two-week and four-week follow-up periods.
- To document and analyze the frequency of adverse events associated with itraconazole in the treatment of Tinea Corporis.

METHODS & MATERIAL

This study employed a cross-sectional prospective design to assess the effectiveness and safety of itraconazole in treating Tinea corporis across different age groups, in the Department of Dermatology, Mymensingh Medical College and Hospital, Mymensingh, Bangladesh, from July 2023 to January 2024. Participants provided informed consent before their inclusion in the study. A total of 472 patients were selected for his study. Participants were recruited from dermatology outpatient clinics from multiple centers spread across diverse geographic locations. This strategy was chosen to ensure the study population accurately reflected the variability in climate and environmental factors that could influence the epidemiology and treatment outcomes of Tinea corporis.

Inclusion Criteria:

- Clinically diagnosed with Tinea corporis, confirmed by direct microscopic examination and culture of skin scrapings.
- Aged between 2 to 75 years.
- Willing and able to provide informed consent, or for minors, consent provided by a parent or guardian.
- Able and willing to comply with study requirements, including follow-up visits and treatment protocol.

Exclusion Criteria:

- Use of systemic or topical antifungal treatment within the two weeks before enrollment.
- History of pre-existing heart disease.
- History of chronic liver disease or abnormal liver function tests.
- Currently pregnant or breastfeeding.
- Known hypersensitivity or contraindication to itraconazole or other similar class antifungal medications.
- The presence of immunocompromising conditions, such as HIV/AIDS or systemic corticosteroid therapy, could affect the natural

course of Tinea corporis or its response to treatment.

- Presence of other dermatological conditions that could interfere with the diagnosis and assessment of Tinea corporis.

Data were collected at the initial visit and included demographic information, detailed medical and dermatological history, and specific details about the Tinea corporis infection (e.g., duration, previous treatments, and lesion characteristics). Treatment outcomes were assessed through follow-up visits scheduled two weeks after the initial dose of itraconazole and a final evaluation at four weeks. Efficacy was measured by changes in clinical appearance and symptoms, while safety was assessed by monitoring adverse events reported by participants. All participants received itraconazole at a standard dose adjusted for body weight and age, following existing guidelines. No placebo or control medication was used, as the primary aim was to evaluate the treatment within a real-world setting across diverse demographic groups. Descriptive statistics were used to characterize the study population. The effectiveness of itraconazole was analyzed using a before-and-after comparison within the same population, examining the clearance of fungal lesions and symptom resolution. Safety analysis focused on the incidence and type of adverse effects reported. Data were analyzed using SPSS and significance was set at $p<0.05$.

RESULTS

Table I: Demographics and Baseline Characteristics of the Patients (*n*=472)

Characteristic	Total (*n*=472)	Children (2-12)	Adolescents and Young Adults (13-35)	Middle-Aged Adults (36-60)	Elderly (>60)
Number of Participants	472	94 (20%)	189 (40%)	142 (30%)	47 (10%)
Gender (Male/Female)	255/217	50/44	102/87	78/64	25/22
Duration of Infection	-	2.4 ± 1.5 weeks	2.1 ± 1.3 weeks	2.3 ± 1.4 weeks	2.2 ± 1.0 weeks

The table categorizes participants into four age groups: children aged 2-12 (94, 20%), adolescents and young adults aged 13-35 (189, 40%), middle-aged adults aged 36-60 (142, 30%), and elderly over 60 years (47, 10%). Gender distribution is also detailed for each group, with 255 males and 217 females overall: 50 males and 44 females among children, 102 males and 87 females in adolescents and young adults, 78 males and 64 females in middle-aged adults, and 25 males and 22 females in the elderly. The duration of infection before the study is reported as averages with standard deviations: 2.4 ± 1.5 weeks for children, 2.1 ± 1.3 weeks for adolescents and young adults, 2.3 ± 1.4 weeks for middle-aged adults, and 2.2 ± 1.0 weeks for the elderly. [**Table I**]

Table II: Lesion Response at Two-Week Follow-Up (*n*=472)

Age Group	Complete Clearing (%)	Significant Improvement (%)
Children (2-12)	58 (55/94)	35 (33/94)
Adolescents and Young Adults (13-35)	60 (113/189)	32 (61/189)
Middle-Aged Adults (36-60)	65 (92/142)	28 (40/142)
Elderly (>60)	67 (32/47)	25 (12/47)

For children aged 2-12, 58% (55 out of 94) experienced complete clearing of their lesions, and 35% (33 out of 94) showed significant improvement. In the adolescents and young adults group (13-35 years), 60% (113 out of 189) achieved complete clearing, while 32% (61 out of 189) noted significant improvement. Among middle-aged adults (36-60 years), 65% (92 out of 142) saw complete clearing of lesions, and 28% (40 out of 142) had significant improvement. Lastly, in the elderly group (over 60 years), 67% (32 out of 47) achieved complete clearing, with 25% (12 out of 47) showing significant improvement. [**Table II**]

Table III: Final Outcomes at Four-Week Follow-Up (*n*=472)

Age Group	Complete Clearing (%)	*p*-value
Children (2-12)	82 (77/94)	<0.01
Adolescents and Young Adults (13-35)	86 (163/189)	<0.01
Middle-Aged Adults (36-60)	89 (126/142)	<0.01
Elderly (>60)	88 (41/47)	<0.01

In the children group (ages 2-12), 82% (77 out of 94) reached complete clearing, with a p-value of less than 0.01, indicating a statistically significant improvement. Similarly, 86% (163 out of 189) of adolescents and young adults (ages 13-35) showed complete clearing, with the same level of statistical significance. Among middle-aged adults (ages 36-60), the highest response was observed, with 89% (126 out of 142) achieving complete clearing, also significant at a p-value of less than 0.01. The elderly group (over 60 years) also demonstrated high efficacy, with 88% (41 out of 47) showing complete clearing, supported by a statistically significant p-value of less than 0.01. [**Table III**]

Table IV: Symptom Resolution Over Time (*n*=472)

Follow-Up Period	No or Minimal Symptoms (%)
Two Weeks	70 (330/472)
Four Weeks	90 (425/472)

The data is summarized at two distinct follow-up intervals: two weeks and four weeks. After two weeks of treatment, 70% (330 out of 472) of participants reported experiencing no or minimal symptoms. This improvement was more pronounced by the four-week mark, with 90% (425 out of 472) of participants noting no or minimal symptoms. [**Table IV**]

Table V: Comparison of Efficacy by Age Group (*n*=472)

Age Group	Complete Clearing at Four Weeks (%)	p-value
Children (2-12)	82 (77/94)	>0.05
Adolescents and Young Adults (13-35)	86 (163/189)	>0.05
Middle-Aged Adults (36-60)	89 (126/142)	>0.05
Elderly (>60)	88 (41/47)	>0.05

In this study 82% (77 out of 94) of children aged 2-12, 86% (163 out of 189) of adolescents and young adults aged 13-35, 89% (126 out of 142) in middle-aged adults, and 88% (41 out of 47) in the elderly experienced complete clearing. Across all age groups, the p-values were greater than 0.05, indicating that there are no statistically significant differences in the efficacy of itraconazole treatment among these different age demographics based on the four-week data. [**Table V**]

Table VI: Adverse Events Reported (N=472)

Adverse Event	Frequency (%)	Notes
Gastrointestinal Upset	5 (24/472)	Includes nausea and stomach upset
Increased blood pressure	2 (9/472)	Mild increase
Rash	2 (9/472)	Mild, resolved without intervention
Headache	1 (5/472)	Transient, requires no medication
Hearing loss	1 (5/472)	Treatment required

Gastrointestinal upset was the most frequently reported adverse event, occurring in 5% of the participants (24 out of 472), and included symptoms such as nausea and stomach upset. Rash and high blood pressure was reported by 2% of the participants (9 out of 472); these instances were mild and resolved without any medical intervention. Headache was noted by 1% of the participants (5 out of 472), described as transient, and did not require medication. Moreover, 1% (5 out of 472) suffered from hearing loss which required treatment. [**Table VI**]

DISCUSSION

This study aimed to evaluate the efficacy and safety of itraconazole in treating Tinea corporis across different age demographics, which is crucial given the varying physiological responses to treat-

ment observed among age groups. Demographics and baseline characteristics reveal a broad distribution of Tinea corporis across various age groups with a near-equal gender split in this study. This demographic spread is in line with data from Williamson et al., emphasizing that Tinea infections are widespread and indiscriminate of age or gender [13]. The duration of infection before treatment initiation is consistent with those reported by Patel et al., where durations ranged between 2.1 and 2.4 weeks, underscoring the acute nature of these infections [14]. Regarding the lesion response at two-week follow-up, lesion clearing rates were commendable across all age groups at the two-week follow-up, with the highest seen in the elderly at 67%. These results are superior to those reported by Smith and Jones, who noted a maximum clearing rate of 60% in similar follow-up periods [15]. This suggests a potential advantage of the dosing regimen used in our study, tailored to maximize efficacy across different age categories. The complete clearing rates improved significantly at outcomes at a four-week follow-up, aligning with the findings from Rodriguez and Lee [16]. However, our study noted a slightly higher efficacy in the middle-aged group (89%) compared to Rodriguez and Lee's study (84%). The statistical significance of these outcomes ($p<0.01$) underscores the robust effect of itraconazole treatment over time. Symptom Resolution over Time Table IV highlights an impressive progression in symptom resolution, with 90% of participants reporting minimal or no symptoms at four weeks. This significant symptomatic relief surpasses the findings from Lee et al., who reported an 80% reduction [17]. The higher rates observed in our study could be attributed to stringent adherence to treatment protocols and comprehensive patient education. Consistent efficacy across different age groups, with no significant differences ($p>0.05$) was observed in this study, which contrasts with findings from Garcia and Thompson, who reported varying efficacy, particularly noting lower response rates in elderly patients [18]. This discrepancy in results could be attributed to differences in patient selection, dosing regimens, or adherence rates across studies. Similar to our findings, the studies by Morrison et al. and Chen et al. also highlighted uniform efficacy across diverse age groups, supporting the idea that itraconazole can be effectively and uniformly used across all age groups when administered with age-appropriate considerations [19,20]. These studies, together with ours, provide strong evidence that with proper clinical management, itraconazole remains a potent treatment option, irrespective of patient age. Adverse events corroborate the known tolerability of itraconazole, with only minor events like gastrointestinal upset being somewhat common (5%). This incidence is lower than the 8-10% reported in larger cohort studies by Adams and Murray [21]. The minimal nature of the adverse events and their manageable aspect contributes to the high compliance and continuity of therapy observed.

Limitations of the study:

The study has several limitations, including its observational design, which precludes causal inference. The diversity and representativeness of the sample may not fully capture the global population affected by Tinea Corporis. Additionally, the reliance on self-reported data could introduce bias, and the absence of a comparison group limits the robustness of the findings.

Conclusion:

The study demonstrates that itraconazole effectively treats Tinea Corporis across various age groups with consistent efficacy. The results show significant lesion clearance and symptom resolution within four weeks, with no notable differences in response across age demographics. Minimal adverse events further affirm the safety of itraconazole, making it a suitable treatment option for Tinea Corporis universally.

Recommendation:

It is recommended that clinicians consider itraconazole as a preferred treatment for Tinea Corporis across all age groups. Given its high efficacy and low incidence of adverse effects, itraconazole provides a beneficial therapeutic profile. Healthcare providers should ensure appropriate dosing tailored to age-specific needs to maximize outcomes. Continued monitoring and research are advised to further validate these findings and explore the long-term impacts of itraconazole treatment on Tinea Corporis, especially in populations with varied underlying health conditions.

REFERENCES

1. *Elewski BE. Tinea corporis. Clin Mycol. 2008;46(2):321-26.*
2. *Thompson GR, et al. Itraconazole: a comprehensive review. Expert Rev Anti Infect Ther. 2013;11(1):59-79.*
3. *Ryder NS. Mechanism of action and biological profile of antifungal triazole derivatives. Clin Microbiol Rev. 1992;5(2):198-217.*
4. *Gupta AK, et al. Itraconazole for the treatment of pediatric fungal infections: a review. Pediatric Drugs. 2004;6(3):123-42.*
5. *Bellmann R, Smuszkiewicz P. Pharmacokinetics of antifungal agents in onychomycoses. Clin Dermatol. 2010;28(2):217-24.*
6. *Neubert RHH, Gensbügel C. Biopharmaceutical aspects of itraconazole. J Pharm Sci. 2007;96(1):1-12.*
7. *Gupta AK, et al. Pulsed itraconazole treatment in pediatric dermatophytosis. J Am Acad Dermatol. 2007;57(1):99-109.*
8. *Faergemann J, et al. Management of tinea corporis, tinea cruris, and tinea pedis: a comprehensive review. Dermatol Ther. 2016;29(2):124-35.*
9. *Niewerth M, Korting HC. Management of onychomycoses. Drugs. 1999;58(2):283-96.*
10. *Baran R, Faergemann J, Hay RJ. Superficial white onychomycosis—a syndrome with different fungal causes and paths of infection. J Am Acad Dermatol. 2001;45(6):891-96.*
11. *Syed TA, et al. Treatment of tinea capitis with itraconazole capsule pulse therapy. Mycoses. 1998;41(11-12):509-14.*
12. *Krishnan-Natesan S. Resistance of dermatophytes: clinical and mycological implications. Mycoses. 2012;55(4):304-08.*
13. *Williamson DM, et al. Prevalence and demographics of tinea infections. J Clin Microbiol. 2008;46(8):2493-2496.*
14. *Patel HD, et al. Clinical presentation of tinea infections in dermatology. Dermatology. 2012;225(1):21-24.*
15. *Smith JK, Jones HE. Comparative effectiveness of itraconazole. J Fungal Res. 2015;13(2):58-64.*
16. *Rodriguez RG, Lee SJ. Long-term outcomes in tinea treatment: A comparative analysis. Antifungal Ther. 2017;19(1):67-72.*
17. *Lee DJ, et al. Symptom resolution in fungal infections under varied therapeutic regimens. Mycoses. 2019;62(3):220-227.*
18. *Garcia GS, Thompson LD. Age-related differences in the treatment response to antifungal agents. Gerontol. 2014;60(3):154-159.*
19. *Morrison VA, Johnson E, Whaley FS. Clinical implications of age-related differences in the primary treatment of fungal infections. J Gerontol A Biol Sci Med Sci. 2017;72(3):333-338.*
20. *Chen XY, Kim P, Farahnik B. Efficacy of antifungal treatments in elderly populations: a systematic review. J Clin Pharm Ther. 2018;43(5):624-630.*
21. *Adams KT, Murray R. Adverse events associated with itraconazole in dermatological use: A retrospective study. Drug Saf. 2021;44(4):451-457.*