Randomized Control Trial of Itraconazole in the Treatment of Dermatophytosis: Comparison of Three Different Dose Regimens

Abhishek Chandrakant Lachure, Bhabani S. T. P. Singh, Bikash Ranjan Kar, Liza Mohapatra, Nibedita Dixit

Department of DVL, Institute of Medical Sciences and SUM Hospital, SOA University, Bhubaneswar, Odisha, India

Abstract

Introduction: Dermatophytosis is a superficial fungal infection of keratinized tissue caused by dermatophytes. The use of itraconazole in the standard dose and duration is commonly resulting in treatment failure. **Aims and Objectives:** To compare the efficacy and safety of three different dosage regimens of itraconazole in the treatment of dermatophytosis. **Materials and Methods:** Patients were enrolled and randomly assigned to three different groups A, B, and C after obtaining the proper consent. For four weeks, patients in Groups A, B, and C received itraconazole 100 mg once daily, 200 mg once daily, and 5 mg/kg or 400 mg daily, whichever was lesser, in two divided doses, respectively. All patients were advised to use topical eberconazole cream twice daily and levocetirizine 5 mg daily. Potassium hydroxide (KOH), culture for fungus, complete blood count (CBC), and liver function test (LFT) were done at the baseline visit and repeated in 4 weeks. A clinical assessment was done at both visits. **Result:** KOH was negative for fungal elements in 21.4%, 19%, and 17% of patients in groups A, B, and C respectively, after the completion of therapy. The culture was negative for fungal elements in 19%, 17.5%, and 19.5% of patients in groups A, B, and C respectively, post-therapy. At the end of four weeks, there was a statistically significant decrease in lesion count, body surface area involvement, erythema, and itching within all three groups. However, after 4 weeks of therapy, there was no significant difference in clinical outcome or mycological status among the three groups. **Conclusion:** Our study concludes that the higher dose of itraconazole does not prove to be more efficacious and has no added advantage over the conventional dose in the treatment of dermatophytosis at the end of four weeks. Therefore, we suggest for long-term (more than 4 weeks) itraconazole therapy with the conventional dose to achieve an adequate cure.

Keywords: Antifungal, azoles, different dose regimens, efficacy, safety, superficial fungal infection

Introduction

Dermatophytosis is a superficial fungal infection of keratinized tissue caused by dermatophytes. The disease has a significant negative impact on social, psychological, and occupational health.[1] Studies have shown an increasing burden of dermatophytosis in the general population.[2] There is an epidemic of recurrent and chronic dermatophytosis in India.[3] Among the systemic antifungals, itraconazole is the most commonly used drug in the treatment of dermatophytosis. The textbook recommended dose of itraconazole is 100 mg per day for 2–4 weeks.[4] The doses of itraconazole have also been mentioned as 200 mg per day for 1 week.[5] However, failure of treatment is being increasingly seen with the use of itraconazole in conventional doses and duration. An inappropriate dose or duration of itraconazole may lead to a partial response, rapid recurrence of infection, and the development of drug resistance.[6] The risk of adverse effects due to the use of higher doses of itraconazole also

Submission: 29-10-2022 **Revision:** 18-11-2022
Acceptance: 02-12-2022 **Web Publication:** 17-06-2023

Access this article online

Quick Response Code:

Website: www.tjdonline.org

DOI: 10.4103/tjd.tjd_124_22

Address for correspondence: Dr. Bhabani S. T. P. Singh, Department of DVL, Institute of Medical Sciences and SUM Hospital, SOA University, Bhubaneswar, Odisha, India.
E-mail: drbstp@gmail.com

How to cite this article: Lachure AC, S T P Singh B, Kar BR, Mohapatra L, Dixit N. Randomized control trial of itraconazole in the treatment of dermatophytosis: comparison of three different dose regimens. Turk J Dermatol 2023;17:37-43.

exists. Under the prevailing conditions, there is a paucity of literature about the adequate and appropriate dose of itraconazole in tinea. Hence, this study was designed to compare the efficacy and safety of three different dose regimens of itraconazole in the treatment of dermatophytosis.

Aims and Objectives

1. To compare the efficacy of three different dosage regimens of itraconazole in the treatment of dermatophytosis. (100 mg once daily vs 200 mg once daily vs 5 mg/kg or 400 mg daily, whichever is lesser).
2. To compare the safety of three different dosage regimens of itraconazole in the treatment of dermatophytosis.

Materials and Methods

Sample size

The mycological cure rate of dermatophytosis was 70% with a dose of itraconazole 100 mg daily,[7] in comparison to 92% with itraconazole 200 mg daily.[6] We wanted to estimate and compare the cure rate with 400 mg or 5 mg/kg itraconazole. At a 95% confidence interval, with an estimated difference in the proportion of cure rate between the treatment groups of 22%, with an alpha error of 5%, and a beta error of 20%; the sample size was determined to be 35 in each arm. Considering a dropout rate or loss to follow-up of 20%, the sample size was inflated to 42 in each arm. A sample size of 126 (42 in each group) was calculated using the software "P-value: A statistical tool" by Dr. Kusum Gaur.[8] Ethics committee (Ref No/DMR/IMS.SH/SOA/180342) approval was obtained to carry out this study. The trial was registered in the clinical trial registry of India with the CTRI registration number (CTRI/2020/08/027063). The study was carried out from September 2020 to October 2021.

Inclusion criteria

1. All naive cases of dermatophytosis.
2. Positive cases with fungal hyphae on potassium hydroxide (KOH) test.
3. Patients aged 18 to 60 years.
4. Previously treated cases but off treatment from topical/systemic antifungal since last 4 weeks.

Exclusion criteria

1. Pregnant or lactating patient.
2. Patients with a history of diabetes or immunosuppression.
3. Patients taking drugs that interfere with itraconazole metabolism.
4. History of hepatic and renal impairment.
5. Known cases of congestive heart failure

Methodology

Detailed consent in both English and the local language was taken from the patient before enrolling them in the study. Then, the patients were randomly assigned to different groups based on a computer-generated random number table. For four weeks, group A patients received 100 mg of itraconazole once daily, group B patients received 100 mg twice daily, and group C patients received 5 mg/kg or 400 mg daily (whichever was less) in two divided doses. All the participants were prescribed topical eberconazole cream to be applied twice daily on the affected area and a tablet of levocetirizine 5 mg daily for 4 weeks. All patient samples (skin scraping) were sent for potassium hydroxide (KOH) and culture, along with a complete blood count (CBC) and liver function test (LFT) at baseline and again at the end of the 4th week [Figure 1].

Assessment tool

Direct microscopic examination (KOH), culture, and clinical photographs of both visits were compared. Grading of clinical parameters was done by the measurement of body surface area (BSA) involved, while the erythema was measured at both visits on a scale of 0–3 (0-absent, 1-mild, 2-moderate, and 3-severe), and the itching was quantified by the visual analog scale (VAS) (0–10).

Statistics

The information was entered into Microsoft Excel 2007 and analyzed using SPSS version 27 (IBM corporation, Armonk, New York). The categorical variables were expressed in terms of their numbers and percentages, whereas, continuous variables were expressed in terms of their mean and standard deviation. The association of two categorical variables among the groups was obtained using the Chi-square test, whereas, within the groups, an association was obtained using McNemar's test. An association between continuous variables between two independent groups was obtained using an unpaired t-test. A P-value of less than 0.05 was considered statistically significant.

Result

The demographic profile (age/gender) was comparable among all the participants. The mean age ± SD (in terms of years) was 32.88 ± 9.26, 34.74 ± 10.16, and 37.17 ± 6.18 in groups A, B, and C respectively (P = 0.081). Male to female ratio in groups A, B and C was 19:23, 26:16, and 27:15 respectively. The gender comparison between the three groups was comparable (P = 0.196). However, the duration of infection among the three groups was not comparable. The mean duration ± SD (in terms of days) of infection in group B was 88.10 ± 71.4 while in groups A and C it was 49.93 ± 40.21 and 49.40 ± 33.83 respectively (p-value = 0.001). Clinical features such as the number of lesions, body surface area involvement, and itching as scored

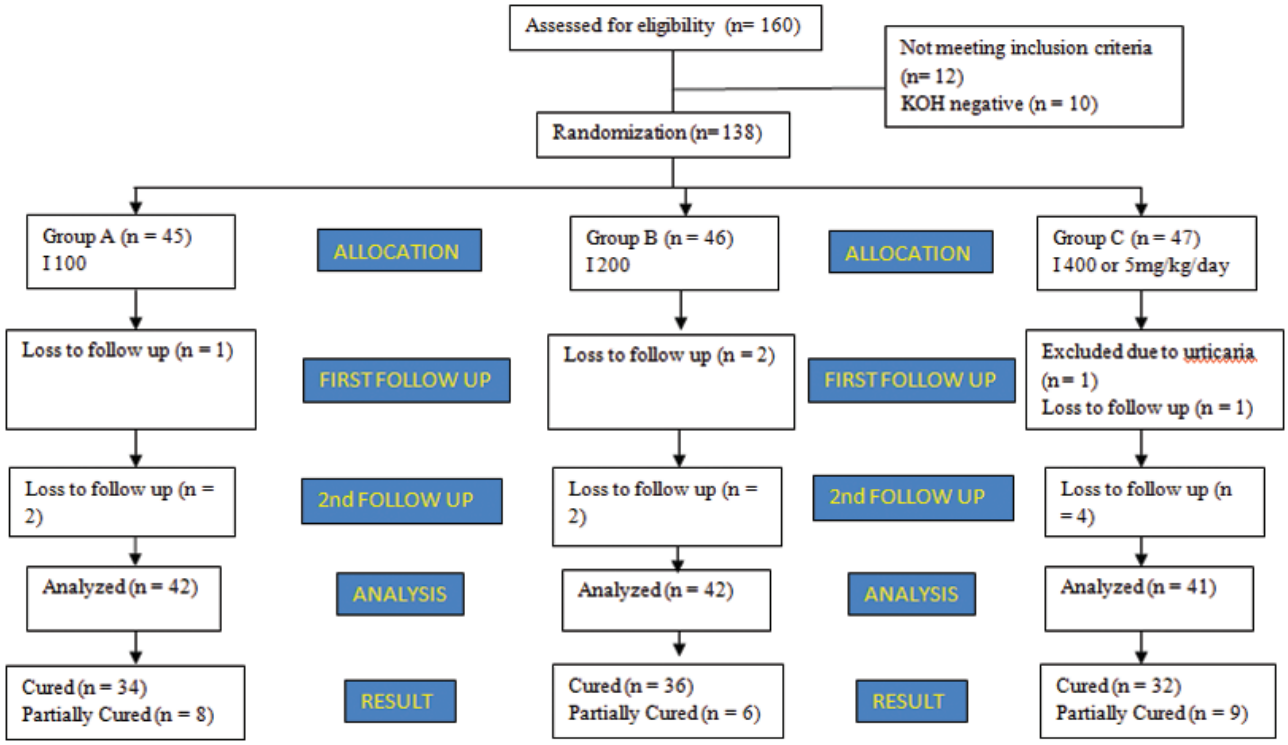

Figure 1: Flow chart depicting passage of participants in the study

on VAS were all comparable among the three groups at the baseline visit [Table 1]. Grading of itching and erythema at the baseline visit was also comparable among the three groups, with p-values of 0.343 and 0.083, respectively.

The decrease in lesion count from the baseline visit was statistically significant in each group at the end of the 4th week with p = < 0.001 [Table 1]. There was no significant difference in the number of lesions at the end of the 4th week when compared among the three groups [Table 1].

There was a statistically significant decrement in the BSA involvement in patients at the end of the 4th week when compared to the baseline in each of the groups with p = < 0.001 [Table 1]. The statistical comparison of BSA involvement at 4 weeks was not significant across the three arms [Table 1].

There was a statistically significant improvement in the VAS of itching post-therapy in all three groups [Table 1]. However, after 4 weeks of therapy, the statistical comparison of VAS of itching was not significant among the three groups [Table 1].

The grading of itching was significantly improved in each group post-therapy, with p-values of 0.027, 0.001, and 0.012 in groups A, B, and C respectively. The grading of erythema also decreased significantly in each group at the end of the therapy with p values of 0.006, 0.006, and 0.004 in groups A, B, and C respectively. However, the inter-group comparison of improvement in the grading of itching (P = 0.53) and erythema (0.753) was not statistically significant, at the end of the intervention.

Table 1: Intra-group and Inter-group comparison of clinical parameters

Number of lesion	Group A	Group B	Group C	*P* value
Baseline	5.55 ± 2.00	6.52 ± 3.44	6.93 ± 3.41	0.103
F/U visit	1.83 ± 1.32	2.38 ± 1.86	2.27 ± 1.94	0.312
	F/U visit	**Baseline Vs F/U visit (*P* value)**		
Group A	1.83 ± 1.32	< 0.001		
Group B	2.38 ± 1.86	< 0.001		
Group C	2.27 ± 1.94	< 0.001		
Body Surface area	**Group A**	**Group B**	**Group C**	***P* value**
Baseline	3.71 ± 1.62	4.55 ± 2.93	4.20 ± 2.70	0.306
F/U visit	0.88 ± 0.83	0.93 ± 0.82	1.04 ± 1.24	0.747
	F/U visit	**Baseline Vs F/U visit (*P* value)**		
Group A	0.88 ± 0.83	< 0.001		
Group B	0.93 ± 0.82	< 0.001		
Group C	1.04 ± 1.24	< 0.001		
VAS of itching	**Group A**	**Group B**	**Group C**	***P* value**
Baseline	7.76 ± 1.36	7.95 ± 1.43	8.36 ± 1.01	0.097
F/U visit	3.00 ± 1.90	3.29 ± 2.06	3.51 ± 1.86	0.487
	F/U visit	**Baseline Vs F/U visit**		
Group A	3.00 ± 1.90	< 0.001		
Group B	3.29 ± 2.06	< 0.001		
Group C	3.51 ± 1.86	< 0.001		

Table 2: Intra-group comparison of KOH and culture

KOH results	Group A		Group B		Group C	
	Baseline	F/U visit	Baseline	F/U visit	Baseline	F/U visit
Positive	42 (100%)	33 (78.57%)	42 (100%)	34 (82.93%)	41 (100%)	34 (82.93%)
Negative	0 (0%)	9 (21.43%)	0 (0%)	7 (17.07%)	0 (0%)	7 (17.07%)
Baseline Vs F/U visit (p value)	0.006		0.023		0.012	
Culture status	**Group A**		**Group B**		**Group C**	
	Baseline	F/U visit	Baseline	F/U visit	Baseline	F/U visit
Positive	42 (100%)	34 (80.95%)	42 (100%)	35 (83.3%)	41 (100%)	33 (78.57%)
Negative	0 (0%)	8 (19.05%)	0 (0%)	7 (17.5%)	0 (0)	8 (19.51%)
Baseline Vs F/U visit (*p* value)	0.012		0.023		0.012	

Table 3: Inter-group comparison of KOH and culture after 4 weeks of therapy

	Group A	Group B	Group C	Total	*P* value
KOH result					
Positive	33 (78.57%)	34 (82.95%)	34 (82.93%)	101 (80.8%)	0.877
Negative	9 (21.43%)	8 (19.05%)	7 (17.07%)	24 (19.2%)	
Culture status					
Positive	34 (82.95%)	35 (83.33%)	33 (80.49%)	102 (81.6%)	0.965
Negative	8 (17.05%)	7 (16.67%)	8 (19.51%)	23 (18.4%)	

A significant number of patients tested negative for fungal elements on KOH smears at four weeks in each of the groups when compared with their baseline status. KOH was negative in 21.4%, 19%, and 17% of patients in groups A, B, and C respectively [Table 2]. There was no significant difference in the conversion of KOH status across the three groups after the completion of therapy, with $P = 0.877$ [Table 3].

There was a statistically significant conversion of culture status in all three groups. Skin scrapping did not yield any fungal growth in 19%, 17.5%, and 19.5% of patients in groups A, B, and C respectively after 4 weeks of therapy [Table 2]. But, the statistical comparison of the culture after 4 weeks of therapy among all three groups was not significant with $P = 0.965$ [Table 3].

In our study, one patient in group C developed urticaria (withdrawn from the study and treated with only oral antihistaminic) and one patient in group A developed an id reaction (treated with the short course oral steroid).

The most common site of persistence of lesions after the 4 weeks of therapy was the groin, followed by the buttock. The statistical comparison of the number of cases with persistent lesions after the therapy among the three groups was not significant.

After 4 weeks of therapy, there was no abnormal derangement of platelet levels in any of the participants. The platelet level at baseline and after 4 weeks of therapy in groups A and C showed a statistically significant decrease with p-value of 0.001 and 0.017 in groups A and C respectively. The decrease in the platelet count was within the physiological limit. There was no significant derangement of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) levels after 4 weeks of therapy in any of the participants at an individual level. But, the statistical comparison of SGPT level at baseline and after 4 weeks of therapy was significant within group C (without any clinical adverse outcome or any biological relevance), indicating a higher dose of itraconazole could lead to derangement of liver enzymes more frequently than the lower dose.

Discussion

Superficial dermatophytosis is considered the most common infective dermatosis in the world, affecting approximately 1/4th of the total world population. The ongoing epidemic of superficial dermatophytosis can be attributed to relapse, recurrence, as well as chronicity. Factors thought to be responsible for the rise in prevalence are inappropriate use of oral and topical antifungals, and rampant misuse of over-the-counter steroid containing mixed creams. In current times, antifungals in their standard doses and duration do not provide a complete cure.[9] According to an Indian study, itraconazole has shown higher clinical and mycological cure rates than terbinafine. With respect to terbinafine therapy, failure rate is high and a longer duration of treatment is required. Therefore, itraconazole is superior to terbinafine in the treatment of superficial fungal infections.[6]

In our study, 57.14% were males and 42.86% were females, with a male-to-female ratio of 1.3:1. This ratio was similar to the findings of previous studies, with a male-to-female ratio

of less than 2.[10-13] The higher prevalence of tinea in males could be explained by factors like increased indulgence in outdoor activities. This exposes them to environmental conditions favorable for the growth of fungus.[11] Higher percentage of patients (44.44%) were in the age group of 31 - 40 years, followed by 34.82%, 17.46%, and 2.38% in 18 - 30 years, 41 - 50 years, and 51 - 60 years respectively. This finding is corroborated by studies conducted by Janardan *et al.*, Singh *et al.* and Agarwal *et al.*[11-13] Such observation could be due to this age group of patients belonging to the working class people with more exposure to humidity and close contact at work. The mean age observed across various studies has been around 31–33 years, which is similar to our study.[10,11] 30.16% of patients were qualified below graduation, whereas 69.84% of patients were graduates or postgraduates, which corresponds to the finding of the study conducted by Kaur *et al.*[14] Similarly, a recent study showed that the majority of their patients had medium educational qualifications (60.20%).[10] Qualified patients, being more aware, and conscious, are motivated to seek medical care, thereby explaining our findings. In our study, a family history of dermatophytosis was present in 42.06% of patients, similar to findings published by Singh *et al.*[11] Dermatophytosis in the study participant was not associated with a positive family history (P value = 0.573). This indicates that the source of infection could be within the family as well as outside the family.

We divided the infection duration into four groups: group I (30 days), group II (30–90 days), group III (> 90 days to 180 days), and group IV (180 days). 73.02% of patients were in group II, followed by 12.5%, 10.32%, and 7.14% in groups I, IV, and III respectively. Chronic dermatophytosis is defined as an infection persisting for more than 6 months with or without recurrence after adequate treatment.[10] In our study, 10.32% of patients had chronic dermatophytosis. In a study, Agarwal *et al.* reported that 62.55% of patients were suffering from dermatophytic infection for more than 3 months.[15]A study in Eastern India revealed that 40.82% of patients were affected with dermatophytosis infection for more than 6 months.[1]

In our study, flexures were more commonly involved than extensors, with 69.84% of patients suffering from the infection in flexures. The majority of patients were suffering from tinea corporis et cruris (64.29%), followed by tinea corporis (19.84%) alone, and tinea cruris (15.87%) alone. The face was one of the affected sites in 7% of patients. In a study by Singh *et al.*, the most common variant detected was tinea corporis along with tinea cruris, followed by tinea corporis alone and tinea cruris alone.[11] Satyendra Singh *et al.* and Verma *et al.* also documented the most common type of tinea to be both tinea corporis et cruris followed by tinea cruris and tinea corporis.[9,10]

24.6% of patients had previously used some topical or oral therapy (1 month before being enrolled in the study) for the treatment of fungal infection. Singh *et al.* reported that 81.7% of patients in their study had previously used any form of medication to get rid of the fungal infection.[9] The patients usually apply steroid-containing mixed cream (due to its availability over the counter) to get symptomatic relief.

Approximately 20% of patients were cured after one month of therapy in all groups [Figures 2,4, and 6]. In

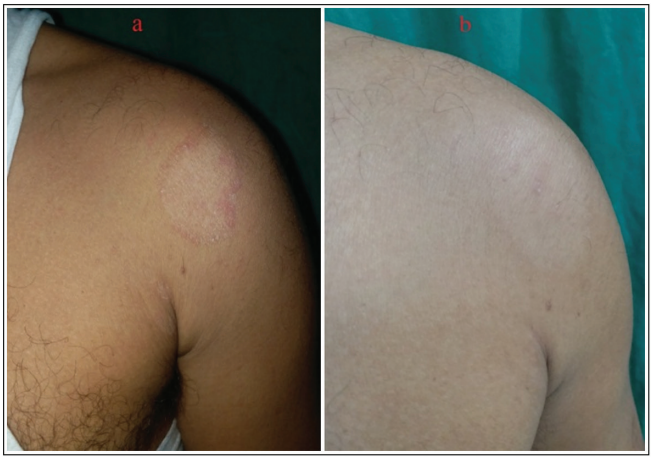

Figure 2: Patient of group A; (a) Lesion at baseline visit, (b) Lesion cleared after 4 weeks of therapy

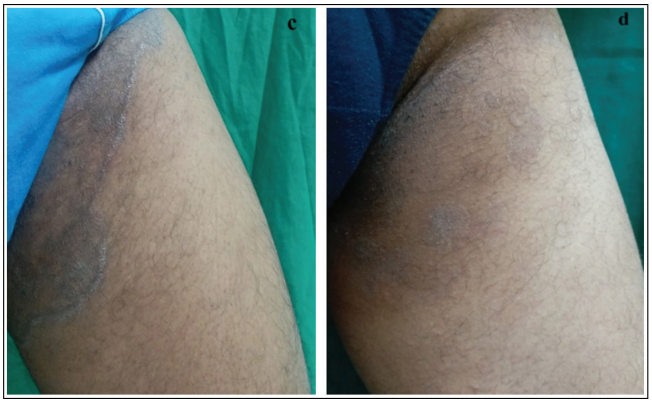

Figure 3: Patient of group A; (c) Lesion at baseline visit, (d) Lesion persisted after 4 weeks of therapy

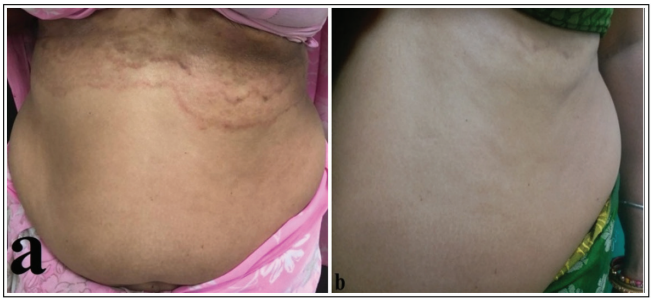

Figure 4: Patient of group B; (a) Lesion at baseline visit, (b) Lesion cleared after 4 weeks of therapy

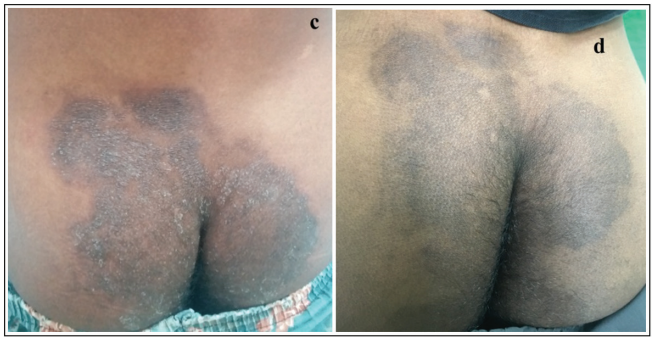

Figure 5: Patient of group B; (c) Lesion at baseline visit, (d) Lesion persisted after 4 weeks of therapy

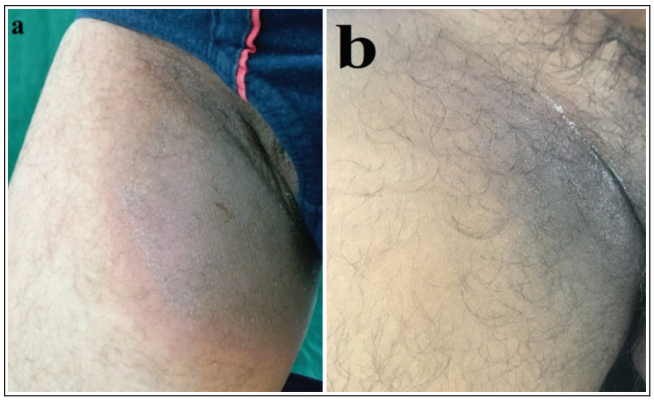

Figure 6: Patient of group C; (a) Lesion at baseline visit, (b) Lesion cleared after 4 weeks of therapy

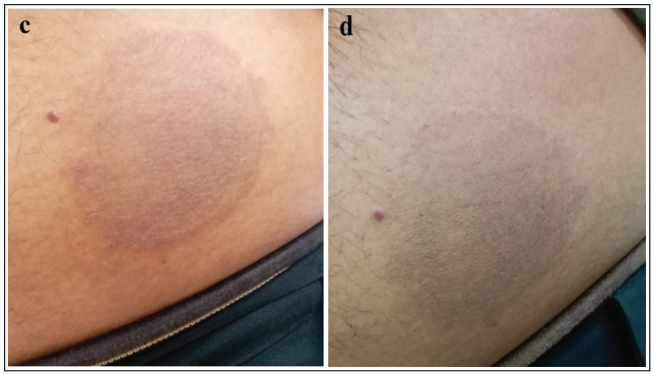

Figure 7: Patient of group C; (c) Lesion at baseline visit, (d) Lesion persisted after 4 weeks of therapy

comparison to the other groups, the remaining patients experienced post-treatment lesion persistence. The groin (47.83%) was the most common site of infection among those with persistent infection, followed by the buttock (43.83%) [Figures 3,5, and 7]. According to a Singh *et al.* study, 20% of patients showed lesion persistence even after being treated with different doses of itraconazole for 4–8 weeks.[9]

21.4%, 19%, and 17% of patients sampled for KOH were negative in the first, second, and third group respectively after 4 weeks of therapy. 19%, 17.5%, and 19.5% of patient's skin samples did not show any fungal growth on culture in the first, second, and third group respectively, after 4 weeks of therapy. The findings of KOH and culture in our study corroborate the finding of a study conducted by Satyendra Singh *et al.*, in which mycological cure was seen in 17% and 19.6% of patients with 200 mg and 400 mg of itraconazole respectively, after 4 weeks of therapy.[9] In a study by M. Haria *et al.*, the mycological cure rate was 65 to 84% after 1–3 weeks of therapy with 200 mg/day of itraconazole.[16] M. Haria conducted this study in 1996. According to H. Degreefe *et al.*'s study, the mycological cure rate was 92% after 4 weeks of 100 mg of itraconazole therapy.[17] However, it is not relevant to our study because this study, with a cure rate of 92%, was conducted in 1987. Frequent recurrences and relapses have been observed with short-term therapy of 100 mg itraconazole.[6] The findings in our study are in contrast to the observation put forth by Sardana *et al.*, that a higher plasma concentration (above 0.2 g/ml) is achieved with 400 mg of itraconazole, which helps to produce a better cure rate in dermatophytosis.[18] In a study, K Sardana and A Khurana reported that even after the use of variable or higher doses of itraconazole, adequate results are not being achieved.[19]

The most common fungal species detected in our study was *Trichophyton rubrum* (56.35%). Skin scraping showed growth of *Trichophyton mentagrophytes, Microsporum canis*, and *Epidermophyton* in 42%, 9%, and 4% of patients respectively. According to an eastern Indian study, the most common dermatophytes causing superficial fungal infection were found to be Trichophyton rubrum and Trichophyton mentagrophytes.[20] However, in another Eastern India study conducted by Singh *et al.*, *Trichophyton mentagrophytes* was found to be the most common fungal species causing dermatophytosis.[11] In a study conducted all over India, it was revealed that the strain responsible for the recent outbreak of superficial fungal infection is Trichophyton mentagrophytes.[21]

In our study, we did not find any significant abnormal derangement of liver enzymes or complete blood count in any of the patients among the three treatment arms at the end of 4th week. Liver enzyme abnormalities are rarely reported due to itraconazole alone. According to Satyendra Singh *et al.*, liver enzyme derangement was seen in only 1.27% of patients due to itraconazole.[9] Star Khoza *et al.* reported the incidence rate of hepatotoxicity as 1 per 10,000 due to itraconazole alone.[22]

Parameters like BSA involvement; total number of lesions; grading as well as the visual analog scale of itching, and the grading of erythema were studied to measure clinical cure in patients. For the mycological cure, skin scrapping for KOH and culture was done. There was no significant difference in the clinical and mycological cure among all three different regimens of itraconazole. Satyendra Singh also reported similar findings.[9]

Conclusion

Statistically significant clinical as well as mycological cure rates were observed with 100 mg, 200 mg, and 400 mg of itraconazole per day at the end of the 4th week. Though the mycological cure was significant with all the dose regimens, the percentage of patients attaining mycological cure was lower. There was no significant derangement of hematologic or hepatic enzyme levels with any of the doses. We propose the need for long-term (more than 4 weeks) itraconazole therapy to achieve adequate mycological cure along with the clinical cure. We conclude that there could be no added advantage of using high-dose itraconazole instead of conventional dose itraconazole in the current scenario of dermatophytosis.

Limitation

The duration of infection among the three groups was not comparable. Follow-up was not done after 4 weeks of study to monitor for the relapse of dermatophytosis.

Acknowledgement

Late Dr Tapaswini Tripathy (M.D), Assistant Professor, Dept. of DVL, IMS & SUM Hospital, SOA university, Bhubaneswar, Odisha, India. She contributed by helping us to achieve the required sample size and also by convincing the subjects to undergo the required investigation at every visit to ensure proper completion of the study.

Author's contribution

Abhishek Lachure – original manuscript writing, review and editing, data curation, literature search. Bhabani S.T.P Singh – original manuscript writing, data curation, statistical analysis, design. Bikash Kar – conceptualization, design, validation, reviewing. Liza Mohapatra – supervision, review and editing, validation. Nibedita Dixit – data curation, review and editing, statistical analysis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Data availibility statement

All the research data referred for this study can be directly accessed through the references provided at the end of the main manuscript.

References

1. Patro N, Panda M, Jena AK. The menace of superficial dermatophytosis on the quality of life of patients attending referral hospital in eastern india: A cross-sectional observational study. Indian Dermatol Online J 2019;10:262-6.
2. Verma S, Madhu R. The great indian epidemic of superficial dermatophytosis: An appraisal. Indian J Dermatol 2017;62:227-36.
3. Sharma R, Adhikari L, Sharma RL. Recurrent dermatophytosis: A rising problem in sikkim, a himalayan state of India. Indian J Pathol Microbiol 2017;60:541-5.
4. Hay RJ, Ashbee HR. Fungal infections. In: Griffiths CE, Barker J, Bleiker T, Chalmer R, Creamer D, editors. Rook's textbook of Dermatology. 9th ed, Vol 2. West Sussex: Wiley Blackwell; 2016. p. 923-1018.
5. Elewski BE, Hughey LC, Sobera JO, Hay R. Fungal diseases. In: Bolognia JL, Jorizzo JL, Schaffer JV, editors. Dermatology. 3rd ed, Vol 2. China: Elsevier Saunders. 2012. P. 1267.
6. Bhatia A, Kanish B, Badyal DK, Kate P, Choudhary S. Efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin - A prospective, randomized comparative study. Indian J Pharmacol 2019;51:116-9.
7. Boonk W, de Geer D, de Kreek E, Remme J, van Huystee B. Itraconazole in the treatment of tinea corporis and tinea cruris: Comparison of two treatment schedules. Mycoses 1998;41:509-14.
8. Kusum Gaur. P value: A statistical tool app. Version 1.4. www.drkusumgaur.com, https://appagg.com/29900221. [Last accessed 9 February 2020].
9. Singh SK, Subba N, Tilak R. Efficacy of terbinafine and itraconazole in different doses and in combination in the treatment of tinea infection: A randomized controlled parallel group open labeled trial with clinico-mycological correlation. Indian J Dermatol 2020;65:284-9.
10. Verma SB, Panda S, Nenoff P, Singal A, Rudramurthy SM, Uhrlass S, *et al*. The unprecedented epidemic-like scenario of dermatophytosis in india: I. Epidemiology, risk factors and clinical features. Indian J Dermatol Venereol Leprol 2021;87:154-75.
11. Singh BSTP, Tripathy T, Kar BR, Ray A. Clinicomycological study of dermatophytosis in a tertiary care hospital in eastern india: A cross-sectional study. Indian Dermatol Online J 2020;11:46-50.
12. Agarwal US, Saran J, Agarwal P. Clinico-mycological study of dermatophytes in a tertiary care centre in northwest India. Indian J Dermatol Venereol Leprol 2014;80:194.
13. Janardhan B, Vani G. Clinico mycological study of dermatophytosis. Int J Res Med Sci 2017;5:31-9.
14. Kaur R, Panda PS, Sardana K, Khan S. Mycological pattern of dermatomycoses in a tertiary care hospital. J Trop Med 2015;2015:157828.
15. Rakosi T, Gerber M. Treatment of tinea with itraconazole: An open multicentre study. Journal of Dermatological Treatment 1995;6:35-8.
16. Haria M, Bryson HM, Goa KL. Itraconazole. A reappraisal of its pharmacological properties and therapeutic use in the management of superficial fungal infections. Drugs 1996;51:585-620.
17. Degreef H, Mariën K, De Veylder H, Duprez K, Borghys A, Verhoeve L. Itraconazole in the treatment of dermatophytoses: A comparison of two daily dosages. Rev Infect Dis 1987;9 Suppl 1:S104-8.
18. Khurana A, Agarwal A, Singh A, Sardana K, Ghadlinge M, Agrawal D, *et al*. Predicting a therapeutic cut-off serum level of itraconazole in recalcitrant tinea corporis and cruris-A prospective trial. Mycoses 2021;64:1480-8.
19. Khurana A, Sardana K. Reinterpreting minimum inhibitory concentration (MIC) data of itraconazole versus terbinafine for dermatophytosis - time to look beyond the MIC data? Indian J Dermatol Venereol Leprol 2018;84:61-2.
20. Hazarika D, Jahan N, Sharma A. Changing trend of superficial mycoses with increasing nondermatophyte mold infection: A clinicomycological study at a tertiary referral center in Assam. Indian J Dermatol 2019;64:261-5.
21. Nenoff P, Verma SB, Vasani R, Burmester A, Hipler UC, Wittig F, *et al*. The current indian epidemic of superficial dermatophytosis due to trichophyton mentagrophytes-A molecular study. Mycoses 2019;62:336-56.
22. Khoza S, Moyo I, Ncube D. Comparative hepatotoxicity of fluconazole, ketoconazole, itraconazole, terbinafine, and griseofulvin in rats. J Toxicol 2017;2017:6746989.