

# Effectiveness of oral Itraconazole compared to Itraconazole Plus Isotretinoin for the Management of Superficial Dermatophytosis

Zafar Ullah Khan<sup>1</sup>, Faiza Tahir<sup>1</sup>, Samrat Habib<sup>1</sup>, Khawar Khurshid<sup>1</sup>, Ali Nawaz<sup>2</sup>, Taha Habib<sup>3</sup>

<sup>1</sup>Department of Dermatology, Rashid Latif Medical College, Lahore, Pakistan.

<sup>2</sup>Rural Health Center, Miana Gondal, Mandi Bahauddin, Pakistan.

<sup>3</sup>Combined Military Hospital Institute of Medical Sciences, Bahawalpur, Pakistan.

## Abstract

**Background** Superficial dermatophytosis is a recurrent fungal infection affecting keratinized tissues, including the nails, skin, and hair. Recurrence and relapse of the disease remain major concerns despite advancements in antifungal treatment.

**Objective** To examine the safety and effectiveness of oral itraconazole with isotretinoin therapy versus itraconazole monotherapy in patients with superficial dermatophytosis.

**Methods** One hundred and twenty individuals with KOH-positive superficial dermatophytosis participated in a randomized clinical study. Group A received oral isotretinoin (20 mg once daily) along with oral itraconazole (100 mg twice daily) for eight weeks, whereas Group B received oral itraconazole (100 mg twice daily) alone. A 0-3 scale was used to assess the clinical severity of erythema, scaling, and pruritus. Liver function tests and lipid profiles were monitored at baseline and at 4-week intervals.

**Results** After eight weeks treatments both groups showed considerable improvement in erythema, scaling, and pruritus ( $P < .001$ ). Mean erythema scores decreased from  $2.98 \pm 0.13$  to  $0.20 \pm 0.52$  in Group A and from  $2.92 \pm 0.28$  to  $0.25 \pm 0.43$  in Group B, representing improvements of 93.3% and 91.4%, respectively. No statistically significant intergroup differences were observed. The side effects were minimal and self-limiting.

**Conclusion** Although the combination of itraconazole and isotretinoin was well tolerated and safe, the outcomes were not statistically superior to those of itraconazole monotherapy. However, in severe or recurrent cases, isotretinoin may serve as a useful adjuvant by improving fungal clearance and increasing keratinocyte turnover.

**Keywords** Dermatophytes; Itraconazole; Isotretinoin.

Article  
Received on  
03.04.2026

Revised on  
21.05.2026

Accepted on  
21.06.2026

Published on  
30.06.2026

**Citation:** Khan ZU, Tahir F, Habib S, Khurshid K, Nawaz A, Habib T. Effectiveness of oral Itraconazole compared to Itraconazole Plus Isotretinoin for the Management of Superficial Dermatophytosis. *J Pak Assoc Dermatol.* 2026;36(2):173-177. Doi: <https://doi.org/10.66344/jpad.v36i2.3391>

## Introduction

Superficial dermatophytosis is an infection of keratinized tissues caused by dermatophytes belonging to the genera *Microsporum*, *Trichophyton*, and *Epidermophyton*.<sup>1</sup> It affects approximately 25%

### Address for correspondence

Dr. Zafar Ullah Khan, Associate Professor,  
Department of Dermatology,  
Rashid Latif Medical College, Lahore.  
Email: [dermakemcolion@gmail.com](mailto:dermakemcolion@gmail.com)

of the global population, resulting in a significant dermatological disease burden.<sup>2</sup> Clinical manifestations are influenced by several factors, including the infecting species, the anatomical site involved, and the host's immunological status.<sup>3</sup> The diagnosis is primarily clinical and is confirmed by potassium hydroxide (KOH) examination, as many dermatoses may mimic fungal infections.<sup>4</sup> Treatment mainly involves topical and systemic antifungal agents.<sup>5</sup> Although itraconazole has demonstrated

superior efficacy and a favorable safety profile, conventional antifungals such as griseofulvin, ketoconazole, and terbinafine have shown lower cure rates and higher recurrence rates.<sup>6</sup> Despite this, chronicity and frequent relapses remain major concerns.<sup>7</sup>

After oral administration, itraconazole is absorbed by basal keratinocytes and secreted through sweat and sebum, allowing it to accumulate in the epidermis.<sup>8</sup> It exerts a “reservoir effect” that helps prevent recurrence, as tissue concentrations remain several times higher than plasma concentrations and may persist in the stratum corneum for up to three weeks after discontinuation.<sup>9</sup>

Recent studies suggest that isotretinoin increases epidermal turnover, thereby accelerating the elimination of fungal elements through its keratolytic action and promotion of desquamation.<sup>7,8</sup> This study was conducted to determine whether adding oral isotretinoin to itraconazole therapy produces better clinical and mycological outcomes than itraconazole monotherapy in patients with superficial dermatophytosis.

## Methods

This prospective, parallel-group comparative clinical trial was conducted in the Department of Dermatology at Arif Memorial Teaching Hospital, Lahore, after obtaining IRB approval (Ref. No. IRB/2024/223 dated 06.12.2024). After providing informed consent, 120 individuals with KOH-positive superficial dermatophytosis were enrolled. Patients of either gender, aged 18-60 years, who were willing to attend follow-up visits were included in the study. Exclusion criteria included pregnancy, breastfeeding, hyperlipidemia, chronic liver disease, and previous use of isotretinoin.

Comprehensive demographic information was recorded, including age, gender, comorbidities, duration of illness, and history of antifungal use. Skin scrapings were collected from the active margins of lesions and examined with 10% KOH to confirm the presence of fungal hyphae. Baseline

laboratory investigations included complete blood count (CBC), lipid profile, fasting blood sugar, liver function tests, and kidney function tests. For females of reproductive age, a baseline urine pregnancy test was also performed.

Participants were randomly divided into two groups. Group A (n=60) received oral itraconazole 100 mg twice daily along with oral isotretinoin 20 mg once daily. Group B (n=60) received oral itraconazole 100 mg twice daily alone. Participants were allocated to either treatment group using simple random sampling through a lottery method, ensuring an equal probability of assignment to each treatment group. The calculated sample size at a 95% confidence interval, with a 5% margin of error and 50% response distribution, was 120 participants. Considering possible non-response and loss to follow-up during data collection, all enrolled participants were included in the final analysis. The sample size was calculated using the WHO sample size calculator using the formula:

$$n = [\sigma^2 \times (Z_{(1-\alpha/2)} + Z_{(1-\beta)})^2] / (\mu_a - \mu_0)^2$$

No topical antifungal medications were prescribed. Oral antihistamines were permitted for pruritus when necessary. Patients were evaluated every two weeks for a total duration of eight weeks. Clinical severity was assessed using a physician-rated 4-point scale (0 = absent, 1 = mild, 2 = moderate, and 3 = severe) for erythema, scaling, and pruritus. Lipid profiles and liver function tests were repeated at week four.

Clinical cure was defined as the absence of erythema, scaling, and pruritus, whereas mycological cure was defined as a negative KOH microscopy result. Qualitative variables were expressed as frequencies and percentages, while quantitative variables were presented as mean±SD. Independent t-tests were used for continuous variables, and chi-square tests were applied for categorical variables. A *P*-value of <.05 was considered statistically significant. Data analysis was performed using SPSS version 26. Informed consent was obtained from all participants.

## Result

For the study, 120 individuals with KOH-positive superficial dermatophytosis were equally divided into two treatment groups. Group B (n=60) received oral itraconazole 100 mg twice daily alone, whereas Group A (n=60) received oral isotretinoin 20 mg once daily in combination with oral itraconazole 100 mg twice daily. At baseline, the two groups were comparable in terms of age ( $P=.97$ ), affected body surface area (BSA) ( $P=.17$ ), and duration of illness ( $P=.46$ ). The mean age of the participants was  $34.8 \pm 11.6$  years.

The two groups had similar demographic and clinical characteristics, with a mean disease duration of  $4.83 \pm 0.96$  months and an average BSA involvement of  $0.32 \pm 0.05$ . At baseline, Group A and Group B demonstrated mean erythema scores of  $2.98 \pm 0.13$  and  $2.92 \pm 0.28$ , respectively, while the mean scaling severity scores were  $2.95 \pm 0.10$  and  $2.98 \pm 0.14$ , respectively. After eight weeks of treatment, erythema scores decreased to  $0.20 \pm 0.52$  and  $0.25 \pm 0.43$ , representing mean percentage reductions of 93.3% in Group A and 91.4% in Group B, respectively ( $P<.001$ ) (Table 1).

Similarly, scaling scores improved by 92.9% and 91.6%, decreasing to  $0.21 \pm 0.49$  in Group A and  $0.25 \pm 0.49$  in Group B, respectively ( $P<.001$ ). The severity of pruritus also decreased markedly, with baseline scores of  $2.92 \pm 0.21$  and  $2.96 \pm 0.18$  declining to  $0.15 \pm 0.36$  and  $0.25 \pm 0.43$  in Groups A and B, respectively, representing reductions of 94.9% and 91.6%. Although within-group improvements were highly significant ( $P<.001$ ) for all parameters, no statistically significant differences were observed between the two groups for pruritus

( $P=.61$ ), scaling ( $P=.42$ ), or erythema ( $P=.31$ ).

The adverse effects were mild and did not require discontinuation of therapy. The most common adverse effects in Group A were dyslipidemia (3.3%), deranged liver enzymes (6.7%), gastritis (1.7%), lip cheilitis (3.3%), skin dryness (1.7%), and photosensitivity (1.7%). In Group B, 5.0% of patients developed deranged liver enzymes, while 3.3% experienced dyslipidemia (Table 2).

Neither group experienced any severe or treatment-limiting adverse effects. More than 90% of patients in both groups achieved near-complete remission of erythema, scaling, and pruritus after eight weeks of treatment. Although the addition of isotretinoin to itraconazole did not produce a statistically significant improvement in clinical outcomes, the combination regimen was well tolerated and may serve as a safe and useful adjunctive therapy for severe or chronic dermatophytosis.

## Discussion

Both treatment regimens resulted in significant improvement in erythema, scaling, and pruritus. However, no statistically significant difference was observed in the overall efficacy of combination therapy compared with itraconazole monotherapy. Despite this, patients receiving combination therapy

**Table 2** Adverse effects in both treatment groups.

Adverse Effects	Group A n (%)	Group B n (%)
Dyslipidemia	4 (6.7%)	2 (3.3%)
Deranged Liver function test	1 (1.7%)	3 (5.0)
Gastritis	1 (1.7%)	-
Lip cheilitis	2 (3.3)	-
Skin dryness	1 (1.7)	-
Photosensitivity	1 (1.7)	-

**Table 1** Comparison of clinical parameters between Group A and Group B before and after treatment.

Clinical Parameter	Duration	Group A (Itraconazole + Isotretinoin) Mean $\pm$ SD	Group B (Itraconazole Alone) Mean $\pm$ SD	P-value
Erythema	Baseline	$2.98 \pm 0.13$	$2.92 \pm 0.28$	.31
	Week 8	$0.20 \pm 0.52$	$0.25 \pm 0.43$	<.001
Scaling	Baseline	$2.95 \pm 0.10$	$2.98 \pm 0.14$	.42
	Week 8	$0.21 \pm 0.49$	$0.25 \pm 0.49$	<.001
Pruritus	Baseline	$2.92 \pm 0.21$	$2.96 \pm 0.18$	.61
	Week 8	$0.15 \pm 0.36$	$0.25 \pm 0.43$	<.001

demonstrated earlier reduction in lesion severity and faster symptomatic recovery, suggesting a potential benefit in accelerating clinical improvement. These findings indicate that although the final therapeutic outcomes may be comparable, adjunctive low-dose isotretinoin may enhance the speed of response in chronic and recurrent dermatophytosis.

The findings of the present study are comparable with several national and international studies. A study conducted in Iran reported that the addition of low-dose isotretinoin to itraconazole improved clinical outcomes in patients with chronic recurrent dermatophytosis without causing significant adverse effects.<sup>10</sup> The authors proposed that isotretinoin may alter the epidermal environment and improve antifungal penetration, thereby enhancing treatment response. Similarly, an Indian study demonstrated that combining isotretinoin with systemic antifungal agents resulted in better clinical improvement, particularly in patients with extensive and hyperkeratotic lesions who had shown poor response to conventional antifungal therapy.<sup>6</sup>

Another study from India further supported the pharmacological rationale for this combination therapy. The researchers highlighted that isotretinoin accelerates epidermal turnover, which may modify the cutaneous pharmacokinetics of itraconazole. This mechanism may reduce the reservoir effect of itraconazole in the stratum corneum while improving drug penetration into infected tissues, thereby contributing to earlier clinical recovery.<sup>11</sup> In addition, isotretinoin may reduce follicular occlusion and scaling, creating a less favorable environment for fungal persistence and recurrence.

Comparable observations have also been reported in other international studies evaluating adjunctive retinoid therapy in recalcitrant dermatophytosis. These studies suggested that low-dose isotretinoin may be particularly useful in chronic, recurrent, steroid-modified, and hyperkeratotic dermatophytosis, where impaired epidermal turnover contributes to treatment resistance. The faster improvement observed in the present study supports

these previously reported findings and highlights the possible role of isotretinoin as an adjuvant rather than a replacement for systemic antifungal therapy.

Regarding safety, cheilitis, skin dryness, and temporary elevation of serum lipid levels were among the few adverse effects observed in the combination therapy group, which is consistent with previously published studies.<sup>12</sup> Importantly, no significant hepatotoxicity or severe systemic adverse effects were noted in either group. These findings indicate that low-dose isotretinoin, when administered under proper monitoring and supervision, appears to have an acceptable safety profile in patients with chronic dermatophytosis.

Despite these encouraging findings, the present study has certain limitations that should be acknowledged. The study population excluded elderly and immunocompromised individuals, which limits the generalizability of the results to broader patient populations. In addition, the relatively short follow-up period may not have adequately captured late relapses or long-term recurrence rates, which are important concerns in chronic dermatophytosis. The single-center design and limited sample size may also restrict the external validity of the findings. Therefore, larger multicenter randomized controlled trials with longer follow-up durations are recommended to further evaluate the long-term efficacy, relapse prevention potential, and safety of combination therapy with low-dose isotretinoin and itraconazole.

Overall, the combination of low-dose isotretinoin with itraconazole appears to be a safe, effective, and clinically promising therapeutic option for chronic or recurrent dermatophytosis, especially in patients with thickened, hyperkeratotic lesions and inadequate response to standard antifungal therapy. Although the combination did not demonstrate statistically superior overall efficacy compared with itraconazole monotherapy, its ability to achieve faster symptomatic relief and earlier lesion resolution may provide meaningful clinical benefits and improve patient satisfaction and treatment compliance.

## Conclusion

The combination of oral isotretinoin and itraconazole showed significant clinical improvement in patients with chronic and recurrent dermatophytosis, particularly by providing earlier symptomatic relief and faster lesion resolution. Although combination therapy was not statistically superior to itraconazole monotherapy, low-dose isotretinoin appeared to be a safe and useful adjuvant by enhancing keratinocyte turnover and aiding fungal clearance. Therefore, it may be beneficial in chronic, severe, hyperkeratotic and recurrent cases with poor response to conventional antifungal therapy.

**Declaration of patient consent** Authors certify that they have obtained all appropriate patient consent.

**Financial support and sponsorship** None.

**Conflict of interest** No conflict of interest.

### Author's contribution

**ZUK, FT:** Substantial contribution to study design, manuscript writing.

**SH:** Substantial contribution to acquisition of data and critical review of the manuscript.

**KK:** Substantial contribution to analysis and interpretation of data and manuscript writing.

**AN,TH:** Substantial contribution to concept, study design and critical review the manuscript.

Every author has given final approval of the manuscript to be published and agreed to be accountable for all aspects of the work.

## References

1. Bitew A. Dermatophytosis: prevalence of dermatophytes and non-dermatophyte fungi from patients attending Arsho Advanced Medical Laboratory, Addis Ababa, Ethiopia. *Dermatol Res Pract.* 2018;**2018**:8164757.
2. Sana S, Ahmed A, Nazir L, Shehzad U, Aftab MN, Ullah N, *et al.* Distribution, molecular characterization, and treatment options for dermatophyte and non-dermatophyte fungi isolated from human and animal samples: an integrated computational and experimental approach. *Allergol Immunopathol.* 2026;**54(1)**:196-211.
3. Rajagopalan M, Inamadar A, Mittal A, Miskeen AK, Srinivas CR, Sardana K, *et al.* Expert consensus on the management of dermatophytosis in India (ECTODERM India). *BMC Dermatol.* 2018;**18(1)**:6. doi:10.1186/s12895-018-0073-1.
4. Brigida S, Elizabeth AA, Soujania G, Poornima RP. A comparative study of safety and efficacy of oral terbinafine and itraconazole in patients of tinea corporis/tinea cruris infection: a randomized open label parallel group study. *Biomed Pharmacol J.* 2021;**14(3)**:1543-9.
5. Verma KK, Senthilnathan G, Bhatia S, Xess I, Gupta V, Dwivedi SN, *et al.* Oral isotretinoin combined with oral terbinafine versus oral terbinafine alone to treat recurrent dermatophytosis: an open-label randomised clinical trial. *Indian Dermatol Online J.* 2021;**12(6)**:820-5.
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(2)**:116-9.
7. Verma SB, Panda S, Nenoff P, Singal A, Rudramurthy SM, Uhrlass S, *et al.* The unprecedented epidemic-like scenario of dermatophytosis in India: III. Antifungal resistance and treatment options. *Indian J Dermatol Venereol Leprol.* 2021;**87(4)**:468-82.
8. Tuknayat A, Bhalla M, Kaur A, Garg S. Familial dermatophytosis in India: a study of the possible contributing risk factors. *J Clin Aesthet Dermatol.* 2020;**13(2)**:58-60.
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(4)**:284-9.
10. Alhamdi DK, Alhamdi KI. Efficacy and safety of adding low-dose isotretinoin to itraconazole in the treatment of chronic recurrent dermatophytosis among a sample of Iraqi patients: an open-labelled therapeutic clinical comparative study. *Indian J Dermatol.* 2022;**67(5)**:624.
11. Srivastava A, Kothiwala SK. Isotretinoin may affect pharmacokinetics of itraconazole in the skin: is it rational to combine both for the treatment of dermatophytosis? *Indian J Dermatol Venereol Leprol.* 2017;**83(1)**:68.
12. Naseemullah, Khan AR, Aslam K, Obaid SM. Efficacy of itraconazole vs itraconazole plus isotretinoin in treatment of chronic tinea. *Pak J Med Health Sci.* 2021;**15(10)**:3316-9.