RESEARCH PAPER

Comparative Efficacy of Oxiconazole Cream Versus Ciclopirox Olamine Cream in the Management of Localized Cutaneous Dermatophytosis: A Randomized Controlled Trial.

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ABSTRACT

Background:Localized dermal infections caused by dermatophytes are a common type of superficial fungal skin infection characterized by inflamed, itchy scaling patches on the skin. Comparing the clinical efficacy of oxiconazole vs ciclopirox olamine in treating dermatophyte infections is limited. This study was designed to evaluate the efficacy and safety of oxiconazole cream compared with ciclopirox olamine cream in the treatment of localized cutaneous dermatophyte infections.

Methods:The study was performed using a randomized controlled trial design at Saveetha Medical College & Hospital in Chennai, India. Forty participants with localized cutaneous dermatophyte infections confirmed clinically and mycologically were enrolled and randomly assigned (1:1) to receive either ciclopirox olamine 1% cream (n=20) or oxiconazole 1% cream (n=20) applied topically twice daily for four weeks. The primary outcome was the percentage change in the total score for all clinical symptoms and signs after four weeks of treatment. Secondary outcomes included treatment response, efficacy, mycological cure rate and adverse events related to treatment. Data were analysed by chi-square analysis for categorical variables and unpaired t-tests for continuous variables with statistical significance defined at $p<0.05$.

Results:Baseline demographic and clinical characteristics were comparable between groups (mean age 32.5±4.3 vs 33.0±3.9 years; p=0.702). Baseline composite scores were 8.3±2.1 in the ciclopirox olamine group and 6.9±1.9 in the oxiconazole group ($p>0.05$). After four weeks of treatment, composite scores reduced to 0.8±0.42 and 1.9±0.99, representing reductions of 93.4% and 72.4%, respectively ($p<0.05$). Mycological cure was achieved in 85% of patients in the ciclopirox olamine group versus 60% in the oxiconazole group ($p<0.05$). Severity improvement to 'none' was observed in 70% of the ciclopirox olamine group versus 30% of the oxiconazole group. Good treatment response was noted in 60% of patients in the ciclopirox olamine group compared to 30% in the oxiconazole group ($p<0.05$). Adverse effects were mild and comparable between groups.

Conclusion:Ciclopirox olamine 1% cream demonstrated superior clinical and mycological efficacy compared to oxiconazole 1% cream in the management of localized cutaneous dermatophytosis. These findings support consideration of ciclopirox olamine as a preferred first-line topical agent. Larger multi-centre trials with longer follow-up are warranted to confirm these findings..

Keywords: Localized cutaneous dermatophytosis; ringworm; ciclopirox olamine; oxiconazole; randomized controlled trial; antifungal treatment; dermatophytes; mycological cure; clinical efficacy

How to cite this article: M SSR, Srinivasan VR, Narasimhalu CRV., Comparative Efficacy of Oxiconazole Cream Versus Ciclopirox Olamine Cream in the Management of Localized Cutaneous Dermatophytosis: A Randomized Controlled Trial..Int J Drug Deliv Technol. 2026; 16(27s): 1-6; DOI: 10.25258/ijddt.16.27s.1

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The infection referred to as dermatophytosis (ringworm) is the most common superficial fungal infection caused by keratin-loving dermatophytes that belong to genera Trichophyton, Microsporum and Epidermophyton. This infection occurs in skin, hair and nail tissues, and is characterized by the chronicity of the infection, recurrence of the infection and a substantial reduction in quality of life. Secondary bacterial infections can develop in severe or neglected cases of dermatophytosis (1-3); thus, a significant portion of dermatology visits in tropical nations (India, for example) are related to superficial fungal infections and, of these, a significant proportion represent dermatophytosis.

Currently, the two major classes of antifungal treatments consist of systemic and topical antifungal medications. Topical antifungal medications are preferred for treating localized dermatophytosis due to greater efficiency, precise targeting, and a lower incidence of systemic side effects. Azole-derivatives and members of the hydroxypyridone

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class are the most frequently used topical antifungal agents. Oxiconazole, which is a member of the imidazole class of antifungal drugs, exerts its antifungal effect by inhibiting the production of ergosterol, which is a critical component of the fungal cell membrane, by inhibiting the enzyme lanosterol 14-alpha-demethylase (4,5). Ciclopirox olamine, which belongs to the hydroxypyridone class of antifungal medications, achieves its antifungal effect through a different mechanism than oxiconazole; ciclopirox olamine exerts its antifungal activity by chelating polyvalent metal cations (e.g., Fe3+ and Al3+) that are essential for the catalysis of many enzymes involved in fungal metabolism and respiration. In addition to ciclopirox olamine's antifungal effect, ciclopirox olamine exerts anti-inflammatory activities that may aid in the acceleration of the resolution of symptoms associated with dermatophytosis (6-8).

Despite the common use of the two topical antifungal agents (oxiconazole and ciclopirox olamine), there is very limited data obtained from comparative, randomized controlled trials (RCT) that provide evidence for the relative clinical and mycological efficacy of each of these agents for treating localized cutaneous dermatophytosis. Therefore, this proposed RCT was designed to fill this lack of evidence by conducting a prospective RCT that compares the safety and efficacy of oxiconazole 1% cream to ciclopirox olamine 1% cream over a course of four weeks of therapy in patients with localized cutaneous dermatophytosis.

Materials and Methods

Study Design and Setting

This was a prospective, open-label, randomized controlled trial conducted at the Dermatology Outpatient Clinic, Saveetha Medical College and Hospital, Chennai, Tamil Nadu, India. The study was registered with the Clinical Trials Registry of India (CTRI) prior to commencement. The protocol was approved by the Institutional Ethics Committee of Saveetha Medical College and Hospital (Ref. No.: [IEC reference number]), and all participants provided written informed consent before enrolment.

Study Population

Adult patients (≥18 years) presenting with localized cutaneous dermatophytosis (tinea corporis, tinea cruris, or tinea faciei) were considered for enrolment.

Inclusion criteria:

Age 18 years and above

Clinical diagnosis of localized cutaneous dermatophytosis (tinea corporis, tinea cruris, or tinea faciei)

Mycological confirmation by positive KOH microscopy and/or positive fungal culture

Willingness to provide written informed consent

Exclusion criteria:

Pregnancy or lactation

Known hypersensitivity to imidazole or hydroxypyridone antifungals

Concurrent use of systemic antifungal agents within four weeks prior to enrolment

Widespread or systemic dermatophytosis requiring systemic therapy

Concurrent immunosuppressive disease or therapy

Tinea unguium (onychomycosis) or tinea capitis

Sample Size and Randomization

A total of 40 eligible patients were enrolled and allocated in a 1:1 ratio to either the ciclopirox olamine group (n=20) or the oxiconazole group (n=20) using block randomization (block size 4) with a computer-generated random number sequence. Allocation concealment was maintained using sequentially numbered opaque sealed envelopes. Although blinding of patients was not feasible given the open-label design, outcome assessors were blinded to group allocation (single-blind).

Interventions

Ciclopirox olamine group: Patients applied ciclopirox olamine 1% cream topically to the affected area(s), covering a margin of approximately 2 cm beyond the lesion border, twice daily for four weeks.

Oxiconazole group: Patients applied oxiconazole 1% cream topically to the affected area(s), with the same application technique, twice daily for four weeks.

Patients were instructed not to use any other topical preparations on the affected areas and were advised on personal hygiene measures to prevent re-infection. Adherence was assessed at follow-up visits by patient self-report and review of the drug supply.

Outcome Measures

Primary outcome: Percentage reduction in the composite clinical symptom and sign score from baseline to week 4. The composite score (0–12) was derived by summing scores for erythema, scaling, pruritus, and lesion size, each graded on a 0–3 scale (0=absent, 1=mild, 2=moderate, 3=severe).

Secondary outcomes: (i) Mycological cure rate (negative KOH microscopy and negative fungal culture at week 4); (ii) severity grade distribution (none/mild/moderate/severe) at baseline and week 4; (iii) overall treatment response categorized as good (score reduction ≥75%), moderate (50–74%), or poor (<50%); and (iv) adverse events.

Statistical Analysis

Quantitative variables are reported as mean ± standard deviation (SD). Qualitative variables are reported as frequency and percentage. The unpaired Student's t-test was used to compare continuous variables between groups. The Chi-square test (or Fisher's exact test where cell counts were <5) was used to compare categorical variables. A two-tailed p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Forty patients with mycologically confirmed localized cutaneous dermatophytosis were enrolled and randomized: 20 to the ciclopirox olamine group and 20 to the oxiconazole group. All 40 patients completed the four-week treatment period and were included in the final analysis. The mean age was 32.5±4.3 years in the ciclopirox olamine group and 33.0±3.9 years in the oxiconazole group

(p=0.702). Gender distribution was 40% male and 60% female in the ciclopirox olamine group versus 30% male and 70% female in the oxiconazole group (p=0.507). Baseline characteristics are summarized in Table 1.

Variable	Ciclopirox olamine cream (n=20)	Oxiconazole cream (n=20)	p-value
Age, years (Mean ± SD)	32.5 ± 4.3	33.0 ± 3.9	0.702
Male : Female	8 : 12 (40% : 60%)	6 : 14 (30% : 70%)	0.507
Tinea corporis, n (%)	10 (50%)	11 (55%)	0.749
Tinea cruris, n (%)	7 (35%)	6 (30%)	0.725
Tinea faciei, n (%)	3 (15%)	3 (15%)	1.000
Baseline composite score (Mean ± SD)	8.3 ± 2.1	6.9 ± 1.9	0.060

SD = standard deviation. p-values from unpaired t-test (continuous variables) or Chi-square test (categorical variables).

Table 2: Composite Clinical Score Before and After Treatment

At baseline, the mean composite clinical score was 8.3±2.1 in the ciclopirox olamine group and 6.9±1.9 in the oxiconazole group, with no statistically significant difference between groups (p=0.06). After four weeks of treatment, the composite score reduced to 0.8±0.42 in the ciclopirox olamine group and 1.9±0.99 in the oxiconazole group. The percentage reduction was 93.4% and 72.4%, respectively, with the difference being statistically significant (p<0.05). These data are presented in Table 2.

Parameter	Ciclopirox olamine cream (n=20)	Oxiconazole cream (n=20)	p-value
Baseline score (Mean ± SD)	8.3 ± 2.1	6.9 ± 1.9	0.060
Post-treatment score (Mean ± SD)	0.8 ± 0.42	1.9 ± 0.99	<0.001
Reduction (%)	93.4%	72.4%	<0.05

p-values from unpaired t-test. Post-treatment p-value reflects inter-group comparison after 4 weeks.

Table 3: Mycological Cure Rates at Week 4

Mycological cure (negative KOH microscopy and negative fungal culture) at week 4 was achieved in 17 of 20 patients (85%) in the ciclopirox olamine group compared to 12 of 20 patients (60%) in the oxiconazole group (p=0.04). These data are presented in Table 3.

Outcome	Ciclopirox olamine cream (n=20)	Oxiconazole cream (n=20)	p-value
KOH negative, n (%)	18 (90%)	13 (65%)	0.031
Culture negative, n (%)	17 (85%)	12 (60%)	0.040
Mycological cure (both negative), n (%)	17 (85%)	12 (60%)	0.040

Mycological cure = negative KOH microscopy AND negative fungal culture at week 4. p-values from Chi-square test.

Figure 1. Mycological cure rates (negative KOH microscopy and culture) at week 4 in both treatment groups.

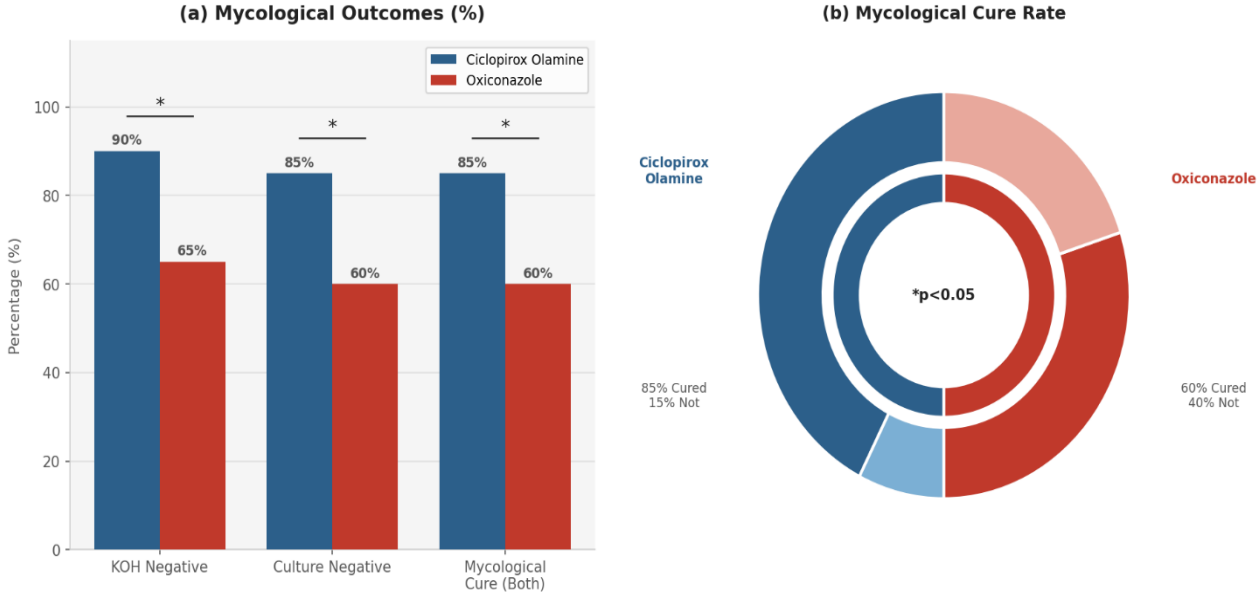

Table 4: Severity Grade Distribution Before and After Treatment

At baseline, severity was comparable between groups, with the majority of patients in both groups having moderate or severe disease. After treatment, 70% of patients in the ciclopirox olamine group achieved complete resolution of symptoms (grade: none), compared to 30% in the oxiconazole group. The distribution of severity grades post-treatment differed significantly between groups ($p<0.05$). Severity data are presented in Table 4.

Severity	Ciclopirox olamine – Baseline	Ciclopirox olamine – Week 4	Oxiconazole – Baseline	Oxiconazole – Week 4
None, n (%)	0 (0%)	14 (70%)	0 (0%)	6 (30%)
Mild, n (%)	2 (10%)	4 (20%)	2 (10%)	8 (40%)
Moderate, n (%)	8 (40%)	2 (10%)	8 (40%)	6 (30%)
Severe, n (%)	10 (50%)	0 (0%)	10 (50%)	0 (0%)

Post-treatment severity distribution between groups: $p<0.05$ (Chi-square test).

Table 5: Overall Treatment Response at Week 4

Based on the percentage reduction in composite score, 60% of patients in the ciclopirox olamine group achieved a good response, compared to 30% in the oxiconazole group. The difference in treatment response distribution was statistically significant ($p<0.05$). Treatment response data are presented in Table 5.

Response	Ciclopirox olamine cream (n=20)	Oxiconazole cream (n=20)	p-value
Good (≥75% reduction), n (%)	12 (60%)	6 (30%)	<0.05
Moderate (50–74% reduction), n (%)	6 (30%)	8 (40%)	
Poor (<50% reduction), n (%)	2 (10%)	6 (30%)	

p-value reflects overall distribution comparison by Chi-square test.

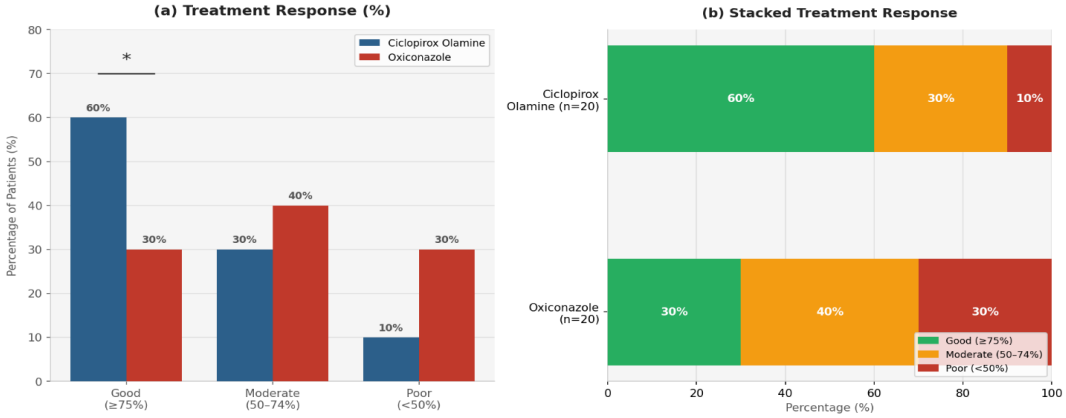

Figure 2. Overall treatment response (good/moderate/poor) at week 4 in the ciclopirox olamine and oxiconazole groups.

Adverse effects were recorded in three patients in the ciclopirox olamine group (mild local burning sensation, n=2; mild erythema at application site, n=1) and in two patients in the oxiconazole group (mild pruritus at application site, n=2). All adverse events were transient, mild in severity, and resolved without treatment discontinuation. No serious adverse events were recorded in either group.

Discussion

This randomized controlled trial compared the clinical and mycological efficacy of ciclopirox olamine 1% cream versus oxiconazole 1% cream over four weeks of treatment in patients with localized cutaneous dermatophytosis. In all the primary and secondary endpoints evaluated, ciclopirox olamine exhibited superior efficacy relative to the control group including: reduction in composite score (93.4% vs. 72.4%), mycological cure (85% vs. 60%), resolution of severity (70% vs. 30% resource-rated as 'none' for both groups) and well-treated response (60% vs. 30%; $p<0.05$).

The superiority of ciclopirox olamine was consistent with its dual mechanism of action. Ciclopirox not only inhibits the function of the fungal membrane by binding metal cations (chelating), but it also possesses anti-inflammatory properties and promotes the early resolution of erythema and pruritus through its independent anti-inflammatory characteristics [9,10]. Jue et al. provided documentation on the broad antimicrobial activity and clinical efficacy of ciclopirox olamine 1% cream for numerous superficial fungal infections, providing a pharmacological basis for our clinical findings [11]. Aly et al. established the bioequivalence of ciclopirox olamine lotion and cream in regard to their pharmacology, thus confirming comparable delivery of the active ingredient between the topical preparations [12].

Oxiconazole, an antifungal agent with established clinical use for dermatophytes, kills dermatophytes by inhibiting the synthesis of ergosterol. Jegasothy and Pakes provided data to document its pharmacology, efficacy, and safety profiles. However, they also indicated that complete resolution of dermatophyte infection may occur over a longer period of time, which is consistent with our findings of decreased short-term efficacy as compared to that of the control group, as evidenced by their lower response rate at four weeks [13]. Gómez-Moyano and colleagues found that ciclopirox olamine 1% cream was safe and effective for treatment of dermatomycosis, including use in children. This is consistent with the safety profile of the drug demonstrated in our study of adults [14].

Group composite scores at baseline were not statistically equivalent between treatment groups ($p=0.06$) but were numerically different (8.34/6.8). Although both treatment groups achieved large absolute reductions in composite scores, it is generally accepted that at baseline, a group with a higher composite score will achieve a larger percentage reduction than will a group with a lower composite score. Thus, this is a recognized limitation of the use of percentage reduction analyses and interpretation of their results between unbalanced baseline groups. However, superiority of ciclopirox olamine was also noted with regard to mycological cure rate-a recovery outcome that was not affected by the magnitude of the baseline score-and therefore provides additional evidence to support the reliability of our conclusion about the clinical value of ciclopirox olamine.

There were nearly no differences between adverse effects of ciclopirox olamine and oxiconazole, and thus continued usage of both agents at the time of study completion was the same. The only adverse reactions were mild local reactions, and no discontinuation of treatment occurred with either agent due to adverse effects [13,14,15].

The present findings support incorporating ciclopirox olamine cream as a preferred topical agent in the management of localized cutaneous dermatophytosis, particularly in settings where rapid and comprehensive symptom resolution is desired. However, larger multi-centre, double-blind RCTs with longer follow-up periods are needed to evaluate recurrence rates and long-term efficacy.

Limitations

The principal limitations of this study include: (i) the relatively small sample size (n=40), which, although adequate for detecting the primary outcome, may limit generalizability; (ii) the open-label design, which precludes blinding of patients and treating physicians, though outcome assessors were blinded; (iii) the conduct at a single centre, which may restrict external validity; (iv) the short four-week treatment and absence of post-treatment follow-up, which preclude assessment of recurrence rates and long-term durability; (v) the moderate baseline score imbalance between groups, which, while statistically non-significant, could partially influence percentage-reduction analyses; and (vi) the absence of species-level identification of causative dermatophytes, which limits assessment of species-specific treatment responses.

Implications

Clinical practice: Ciclopirox olamine 1% cream may be considered a more effective first-line topical option for localized cutaneous dermatophytosis, offering higher clinical and mycological cure rates within a standard four-week treatment course.

Treatment guidelines: Guideline panels may consider incorporating comparative efficacy data from RCTs when recommending between topical antifungal classes for localized dermatophytosis.

Future research: Multicentre, double-blind trials with larger sample sizes, longer follow-up (≥3 months) to capture recurrence, and stratification by dermatophyte species are warranted.

Conclusion

Ciclopirox olamine 1% cream demonstrated significantly superior clinical and mycological efficacy compared to oxiconazole 1% cream over four weeks of treatment in patients with localized cutaneous dermatophytosis, with higher rates of composite score reduction, mycological cure, severity resolution, and good treatment response. Both agents were well tolerated, with only mild and transient local adverse effects. These findings support the use of ciclopirox olamine as a preferred topical antifungal option. Larger, multi-centre, blinded trials with longer follow-up are recommended to confirm these results.

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