

Original Research Article

Effectiveness and safety of eberconazole 1% cream in Indian patients with *Tinea corporis* and *Tinea cruris*: a prospective real-world study

Jayakar Thomas¹, Siddhartha Das², Sunil Ghate³, Manas Chatterjee⁴, Sharad Teltumde⁵,
Sujeet Narayan Charugulla^{6*}, Suyog Mehta⁶, Amey Mane⁶, Rahul Rathod⁶, Ravindra Kale⁶

¹Department of Dermatology, Dr Jayakar Thomas Skin Care Centre, Chennai, Tamil Nadu, India

²Department of Dermatology, Ramkrishna Mission Hospital, Kolkata, West Bengal, India

³Department of Dermatology, Dr. Ghate's Skin, Hair & Laser Center, Mumbai, Maharashtra, India

⁴Department of Dermatology, INHS Asvini Hospital, Mumbai, Maharashtra, India

⁵Department of Dermatology, Sparsh Skin and Dental Clinic, Mumbai, Maharashtra, India

⁶Department of Medical Affairs, Dr Reddy's Laboratories Ltd, Hyderabad, Telangana, India

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*Correspondence:

Dr. Sujeet Narayan Charugulla,

E-mail: sujeetnc@drreddys.com

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ABSTRACT

Background: *Tinea corporis* and *cruris* are estimated to affect 22% to 55% of the Indian population. This real-world study was conducted to evaluate the effectiveness and safety of eberconazole 1% cream among Indian patients.

Methods: In this prospective, single-arm, observational study, patients with *Tinea corporis* and *cruris* aged ≥ 18 years were prescribed eberconazole 1% cream (Ebernet®, Dr. Reddy's Laboratory, India) for up to 3 weeks. The primary endpoint was proportion of patients with improvement in total signs and symptoms score with 2 weeks of treatment. The key secondary endpoint was mean percent reduction in individual signs and symptoms score (erythema, itching, scaling) from baseline to the end of the 1st, 2nd, and 3rd week. A post-hoc analysis was performed on a subgroup of patients (completer set [CS]) who reported application of eberconazole 1% cream for 3 weeks in the study. There were no adverse effects reported.

Results: Of 120 enrolled patients; 104 (86.7%) were included in the full analysis set (FAS) and 76 (63.3%) patients were included in the CS. After 2 weeks of treatment, total signs and symptoms score < 2 was achieved by 25% of patients in the FAS and 28.9% in the CS. After 3 weeks of treatment, mean percent reduction in total sign and symptom score was 60.3% for erythema, 61.2% for itching, and 76.8% for scaling.

Conclusions: The evidence from this real-world observational study and a post-hoc analysis suggests that eberconazole 1% cream is effective and safe treatment option in the management of *Tinea corporis* and *cruris* in Indian patients.

Keywords: Eberconazole, Effectiveness, Real-world, *Tinea corporis*, *Tinea cruris*

INTRODUCTION

Globally, the prevalence of superficial dermatophytes was reported to be 20-25%.^{1,2} However, Indian epidemiology data are scarce and inconclusive. According to the previously published reports,

throughout India incidence of dermatophytosis is $> 36\%$.³ Based on their anatomical location these dermatophytic infections are seen with distinct clinical manifestations. *Tinea corporis* and *Tinea cruris* are superficial dermatophyte infections commonly referred to as ringworm and jock itch, respectively. A study conducted

in Karnataka showed that 53.5% of the included participants had *Tinea corporis* and 25.0% had *Tinea cruris*.⁴ Another study conducted in Tamil Nadu showed much lower prevalence of *Tinea corporis* (25.7%); however, the prevalence of *Tinea cruris* was comparable (23.5%) to that reported in Karnataka.⁵ Recent literature suggested that prevalence of dermatophytosis in Indian patients ranged from 36.6–78.4%.³ The evidence seems definitive about the negative impact of superficial dermatophyte infections on a patient's social and psychological health as well as overall health-related quality of life.^{6,7}

Both *Tinea corporis* and *cruris* are often caused by dermatophytes of the genera- trichophyton, microsporum, and epidermophyton.⁸ Patients with *Tinea corporis* present with lesions that appear as red rings with clear center. These annular lesions may appear anywhere on the body except on the scalp, beard, feet, or hands and are well defined, scaly, and pruritic.⁹ *Tinea cruris* is characterized by red scaling plaques on thighs and inguinal folds and is more prevalent among adolescents and adults.^{9,10}

Most tinea infections are diagnosed based on the clinical manifestations, previous history, and visual examination and rarely laboratory diagnosis using mycological examination is carried out to confirm the diagnosis. But laboratory investigation is preferred in conditions of recalcitrant, chronic and recurrence of the infection. Potassium hydroxide (KOH) microscopy is widely advocated because of more sensitive and reliable than fungal cultures because culture techniques have limited role due to expense and long turnaround time. Molecular diagnosis is helpful to identify subspecies levels of fungi and there are very few centres offering those services in India.¹¹

Oral and topical antifungal agents are the mainstay of *Tinea corporis* and *Tinea cruris* treatment most of the time systemic antifungals therapy is empirically administered.^{10,11} These agents disrupt the synthesis of ergosterol, a vital component of fungal cell membranes, which leads to inhibition of fungal growth.¹² *Tinea corporis* and *cruris* are generally easily manageable with topical antifungals and rarely require systemic therapy.¹³ However, growing evidence highlights the persistence and atypicality of superficial dermatophytes infection in India.¹¹ A significant number of chronic, recurrent, or non-responsive dermatophytosis infections have been observed in the Indian population.^{14,15} This could be due to growing urbanization, overpopulation, poverty, non-adherence to standard care, and other factors related to host immunosuppression like diabetes, HIV/AIDS, and immunosuppressive medications.¹⁶ Currently, limited data is available on effectiveness of different topical antifungal agents due to lack of evidence-based studies.¹⁷

Eberconazole, a topical broad-spectrum imidazole derivative is widely used for the treatment of *Tinea*

corporis and *cruris*.¹⁸ In two independent controlled studies, eberconazole showed similar effectiveness as terbinafine hydrochloride and miconazole.^{11,19} However, unlike other topical azole drugs, evidence for real-world effectiveness and safety of eberconazole in the Indian population with *Tinea corporis* and *Tinea cruris* remains scarce. The present prospective, real-world evidence (RWE) study was conducted to bridge this knowledge gap and generate essential effectiveness and safety data for eberconazole in Indian setting. As loss to follow-up can significantly affect the outcomes of the study in a real-world clinical scenario, a post-hoc analysis was performed on a subgroup of patients who reported use of eberconazole 1% for 3 weeks in the study. This study will provide a valuable reflection of daily clinical practice especially in Indian scenario, where limited RWE data on topical antifungals exists.

METHODS

Study participants

Adult patients (≥ 18 years of age) of either gender who were prescribed eberconazole 1% cream for treatment of *Tinea cruris* and *Tinea corporis* by their treating physician were included in the study. Patients requiring systemic antifungal drugs, pregnant or lactating women, or patients with any significant medical illness such as diabetes, immunocompromised conditions, and other sexually transmitted diseases, etc. that would have prevented study participation, were excluded from the study per Investigator's discretion.

The study was conducted in compliance with the protocol approved by the Institutional review board and/or Independent ethics committee. Written informed consent was obtained from all the patients prior to participation in the study. This study is registered with a clinical trial registry (www.ctri.nic.in) as CTRI/2019/05/019449.

Study design and treatment

This was a prospective, single-arm, observational study conducted between June 11, 2019 and January 09, 2020. Eligible patients were recruited across five centers in India and were prescribed eberconazole 1% cream (Ebernet®, Dr. Reddy's Laboratories Ltd., India) at the discretion of treating physician per approved dosage and frequency of application. Patients were allowed to continue other concomitant medications except systemic antifungal as per their ongoing treatment regimens.

Eligible patient's medical history, demographics, and baseline clinical characteristics including site of lesion, extent of lesion, duration of current illness, clinical symptoms and signs score, treatment history, and number of previous episodes were recorded at baseline (day 1). The overall observation period was 21 days \pm 3 days. Patients were followed-up as per routine clinical practice, and clinical assessments data were collected at baseline

and at weekly intervals from the baseline (1st week [day 7±3], 2nd week [day 14±3] and 3rd week [day 21±3]) for 3 weeks (end of study).

Study endpoints

Primary endpoint of the study was evaluation of the proportion of patients with improvement in total signs and symptoms score from baseline to 2nd week of treatment with eberconazole 1% cream. Improvement criteria was defined as scores ≤2 as ‘improvement’ or >2 as ‘no improvement’. Assessment of individual signs and symptoms (erythema, scaling, and itching) scores was on scale of 0 to 3 (0=absent; 1=mild; 2=moderate; 3=severe).^{18,20,21} Total signs and symptoms score was obtained by addition of individual signs and symptoms score at each time point.

Secondary outcome measures included proportion of patients with improvement of signs and symptoms from baseline to 1st and 3rd week; percent change in signs and symptom score from baseline to 1st, 2nd, and 3rd week; physician’s global assessment of effectiveness and safety at 1st, 2nd, and 3rd week; and patient’s assessment of effectiveness and acceptability at 1st, 2nd, and 3rd week of treatment with eberconazole 1% cream. Physician’s global assessment of effectiveness and safety was graded on a 4-point scale (0=poor, 1=satisfactory, 2=good, and 3=excellent) after 1st, 2nd, and 3rd week of treatment.^{18,20,21} Similarly, patients’ assessment regarding effectiveness and acceptability was also performed. Safety assessment was based on spontaneous adverse event (AE) reported by patients as well as clinicians throughout the observation period (3 weeks).

Analysis set

All the effectiveness analyses performed on the full analysis set (FAS), (i.e. those patients who have received at least one application of medication and completed at

least one post-baseline follow-up visit) were also performed on a subgroup of patients who reported eberconazole topical application for 3 weeks in the study (i.e. the completer set [CS]) in a post-hoc analysis. Safety analysis was performed on all the patients included in the FAS.

Statistical analysis

The primary and secondary effectiveness endpoints were summarized using descriptive statistics; frequencies were reported for categorical variables and means with their standard deviations (SD) and median with range for continuous variables. Difference in proportion of patients with total sign and symptoms scores (based on improvement criteria) were analyzed using Chi square test with a significance level of 0.05. Percentage change in total scores over time with respect to baseline was evaluated using Wilcoxon signed-rank test. Since many patients were discontinued early at the Investigator’s discretion, cure rates for symptoms were computed at each follow-up visit and were presented as numbers with percentages. All the statistical analyses were performed using SAS® (Version 9.4) [SAS Institute Inc., USA]. As loss to follow-up can significantly affect the outcomes of the study in a real-world clinical scenario, a post-hoc analysis was performed on a subgroup of patients who reported use of eberconazole 1% cream for 3 weeks in the study.

RESULTS

Patient disposition and baseline characteristics

Of the 120 patients enrolled in this study, 104 (86.7%) were included in the FAS, and 76 (63.3%) were in the CS. Among the patients who discontinued early (44 [36.7%]), 42 (35%) were lost to follow-up either due to symptom improvements or other unknown reasons, and 2 (1.7%) patients withdrew consent (Figure 1).

Table 1: Demographics and baseline characteristics.

Characteristics	Evaluable population (n=104)
Sex, N (%)	
Men	57 (54.8)
Age (years), mean (SD)	33.7 (13.09)
Body weight (kg), mean (SD)	60.50 (12.56)
Diagnosis, N (%)	
Tinea corporis	44 (42.3)
Tinea cruris	42 (40.4)
Both	18 (17.3)
Number of lesions, median (range)	2 (1-10)
Number of previous episodes of similar lesions, median (range)	1 (1-10)

SD=standard deviation.

Most of the patients were men (54.8%) with a mean (SD) age of 33.7 (13.09) years (Table 1). The primary diagnosis reported 44 (42.3%) patients with tinea corporis, 42 (40.4%) with *Tinea cruris*, and 18 (17.3%)

patients with both. The mean (SD) number of lesions per patient was 2.5 (1.37) and total number of lesions ranged from 1 to 10. A total of 19 (18.2%) patients had previous episodes of similar lesions with a mean (SD) of 2.5 (2.55)

previous lesions per person. Eight patients (7.7%) had at least one prior medication and 57 (54.8%) patients had at

least one concomitant medication (Table 2).

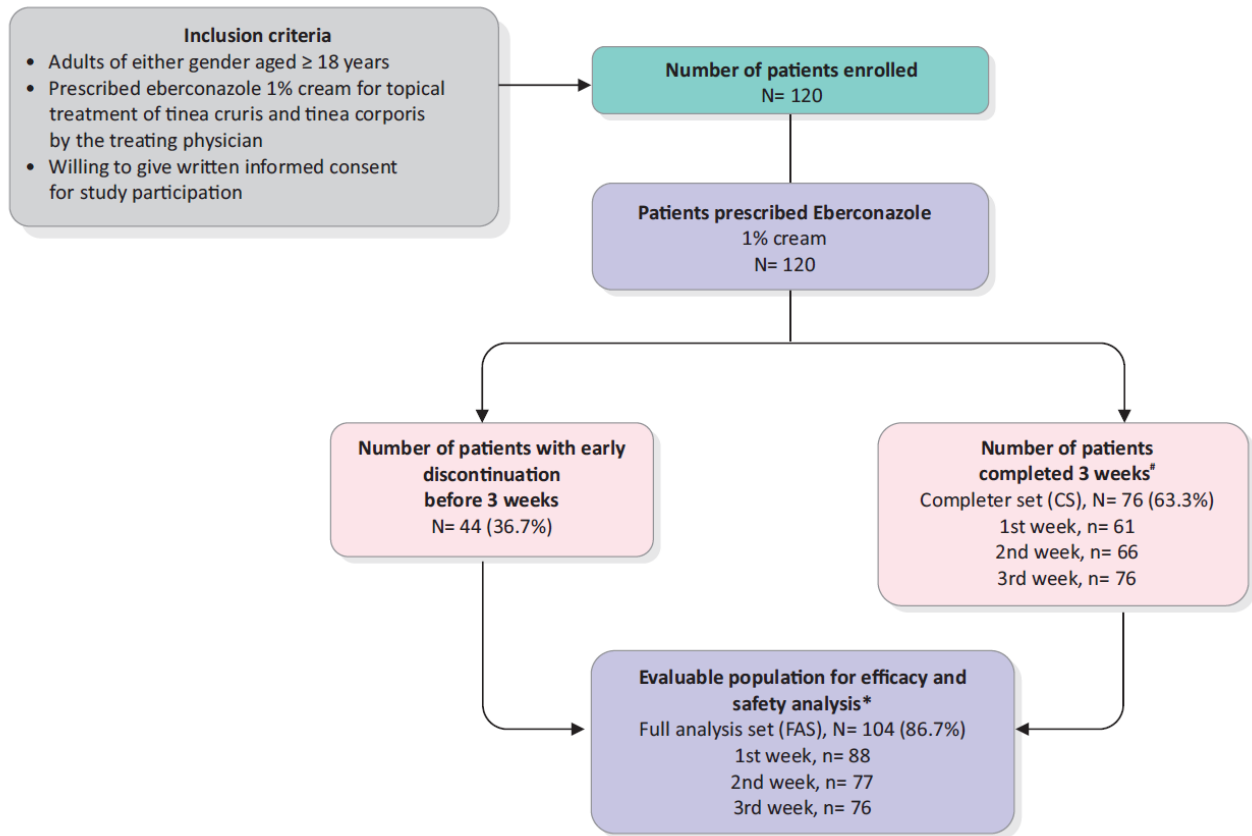


Figure 1: Demographics and baseline characteristics.

#post-hoc analysis of patients who completed 3 weeks in the study; *patients who have received at least one application of medication and completed at least one post-baseline follow-up visit.

Table 2: List of prior and concomitant medication.

Concomitant medications	Evaluable population (n=104)
At least one prior medication*, N (%)	8 (7.7)
Itraconazole	2
Luliconazole	2
Ciclopirox olamine	1
Clotrimazole	1
Amorolfine	1
Fluconazole	1
Miconazole	1
Ketoconazole	1
Clobetasol propionate, Neomycin sulphate, Miconazole nitrate	1
Betamethasone + Clotrimazole	1
At least one concomitant medication#, N (%)	57 (54.8)
Systemic antihistamines, N	
Levocetirizine	19
Bilastine	12
Fexofenadine	12
Hydroxyzine	4
Mizolastine	3
Desolaratidine	2
Ebastine	1

Continued.

Concomitant medications	Evaluable population (n=104)
Topical antifungals, N	
Clotrimazole	4
Luliconazole	1
Amorolfine	1
Terbinafine	1
Topical steroids, N	
Clobetasol propionate	2
Beclometazone dipropionate 0.025% w/v + clotrimazole 1% w/v	1
Other topical agents, N	
Clindamycin	2
Cetrimide	1
Benzoyl peroxide	1
Minoxidil 2% lotion	1
Kojic acid- Dipalmitate	1
Systemic antidiabetic drugs, N	
Metformin + Glimepiride	2
Metformin	1
Linagliptin	1
Systemic hormonal drugs, N	
Thyroxine	2
Cabergoline	1
Progesterone	1
Systemic antihypertensive drugs, N	
Telmisartan	2
Ramipril	1
Tamsulosin	1

*Medications taken up to 30 days prior to first application of eberconazole 1% cream before enrolment in the study are defined as prior medications. #All medications apart from eberconazole 1% cream, for management of *Tinea cruris* and tinea corporis infection as well as other comorbidities were defined as concomitant medication. Note: If patient had more than one concomitant medication that patient is counted for each medication category.

Effiacy assessment

The proportion of patients at follow-up visits with total signs and symptoms score ≥ 2 in the FAS was significantly reduced from baseline to 2nd week of treatment (baseline vs 2nd week: 101 [97.1%] vs 51 [49.0%]; $p < 0.0001$). Similarly, a significant proportion of patients achieved score ≤ 2 at 2nd week with eberconazole 1% cream (baseline vs 2nd week: 3 [2.9%] vs 26 [25.0%]; $p < 0.0001$) (Table 3). A significant proportion of patients achieved score ≤ 2 at the 3rd week in CS too (baseline vs 3rd week: 2 [2.6%] vs 42 [55.3%]; $p < 0.0001$).

Total signs and symptoms score ≤ 2 was significantly ($p < 0.0001$) achieved in 19/104 (18.3%) patients at 1st week, 26/104 (25.0%) patients at 2nd week, and 42/104 (40.4%) patients at 3rd week (Table 3). Mean percent change in total signs and symptoms score from baseline in the FAS was 30% at 1st week, 48.4% at 2nd week, and 68.9% at 3rd week ($p < 0.0001$ at all visits). Mean percent change in total signs and symptoms score was 68.9% in 76 patients in CS at 3rd week. The maximum change in mean (SD) individual signs and symptoms score from baseline was observed at 3rd week, where the score decreased by 1.6 (1.01) for erythema, 1.6 (1.07) for

itching and 1.6 (0.82) for scaling in both FAS as well as CS. Similarly, the maximum mean percent reduction was noted at 3rd week (60.3% for erythema, 61.2% for itching, and 76.8% for scaling) for both the groups. Mean (SD) change and mean percent change in individual signs and symptoms score at every week is presented in Figure 2 and Table 3, respectively. Maximum number of patients had severe symptoms (score 3) at baseline, of which many patients shifted to mild (score 1) to moderate (score 2) intensity or absent signs and symptoms over 3 weeks of treatment (severe symptoms, baseline vs 3rd week:- 68 [65.4%] vs 2 (1.9%) of patients with erythema; 72 [69.2%] vs 9 [8.7%] of patients with itching; 38 [36.5%] vs 0 [0.0%] of patients with scaling) (See Table 5 in the electronic supplementary material for details).

After 3 weeks of treatment, physician's global assessment of effectiveness and safety was reported as good to excellent in 48% of patients in the FAS and 65.8% in the CS, and as satisfactory in 13.5% and 18.4% of the patients in FAS and CS, respectively. Similarly, patient's assessment of effectiveness and acceptability was reported as good to excellent in 43.3% of patients in the FAS and 59.2% in the CS, and as satisfactory in 18.3% and 25% of the patients in FAS and CS, respectively at 3rd week of treatment (Figure 3 and 4).

Table 3: List of prior and concomitant medication.

Summary of assessments	Full analysis set (FAS) (n=104)				Completer set (CS) (n=76)				
	Baseline (n=104)	1st week (n=88)	2nd week (n=77)	3rd week (n=76)	Baseline (n=76)	1st week (n=61)	2nd week (n=66)	3rd week (n=76)	
Proportion of patients with improvement in total sign and symptom scores									
Improvement criteria#									
≤2	N (%)	3 (2.9)	19 (18.3)	26 (25.0)	42 (40.4)	2 (2.6)	7 (9.2)	22 (28.9)	42 (55.3)
>2	N (%)	101 (97.1)	69 (66.3)	51 (49.0)	34 (32.7)	74 (97.4)	54 (71.1)	44 (57.9)	34 (44.7)
	P value*		<0.0001	<0.0001	<0.0001	-	0.0378	<0.0001	<0.0001
Assessment of total sign and symptom scores									
	Mean (SD)	7.0 (1.93)	4.8 (2.27)	3.7 (2.13)	2.3 (2.22)	7.1 (1.88)	5.4 (2.15)	3.7 (2.13)	2.3 (2.22)
Mean % change from baseline									
	%		30.0	48.4	68.9	-	21.7	48.0	68.9
	P value*		<0.0001	<0.0001	<0.0001	-	<0.0001	<0.0001	<0.0001
Assessment of Individual sign and symptom scores									
Mean change from baseline									
Erythema	Mean (SD)	2.4 (1.97)	0.6 (0.73)	1.0 (0.90)	1.6 (1.01)	2.4 (1.00)	0.4 (0.67)	1.0 (0.84)	1.6 (1.01)
Itching	Mean (SD)	2.6 (0.68)	0.9 (0.9)	1.2 (0.93)	1.6 (1.07)	2.6 (0.65)	0.7 (0.91)	1.3 (0.90)	1.6 (1.07)
Scaling	Mean (SD)	2.1 (0.83)	0.8 (0.81)	1.2 (0.80)	1.6 (0.82)	2.1 (0.77)	0.6 (0.76)	1.2 (0.81)	1.6 (0.82)
Mean % change from baseline									
Erythema	%		23.7	39.4	60.3	-	14.5	39.6	60.3
Itching	%		29.7	45.2	61.2	-	21.3	47.5	61.2
Scaling	%		33.0	53.5	76.8	-	21.9	53.5	76.8

SD= standard deviation. * P value is given using Wilcoxon signed-rank test for evaluating percentage change in total scores over time with respect to baseline, # Improvement was assessed based on proportion of patients with sum of total signs and symptom score ≤2.

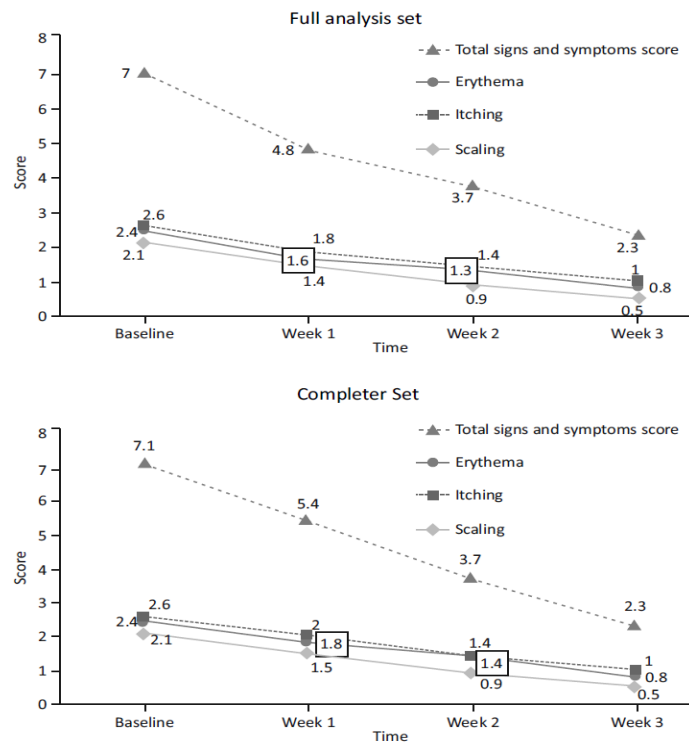


Figure 2: Mean individual signs and symptoms score at baseline and over 3 weeks of treatment.

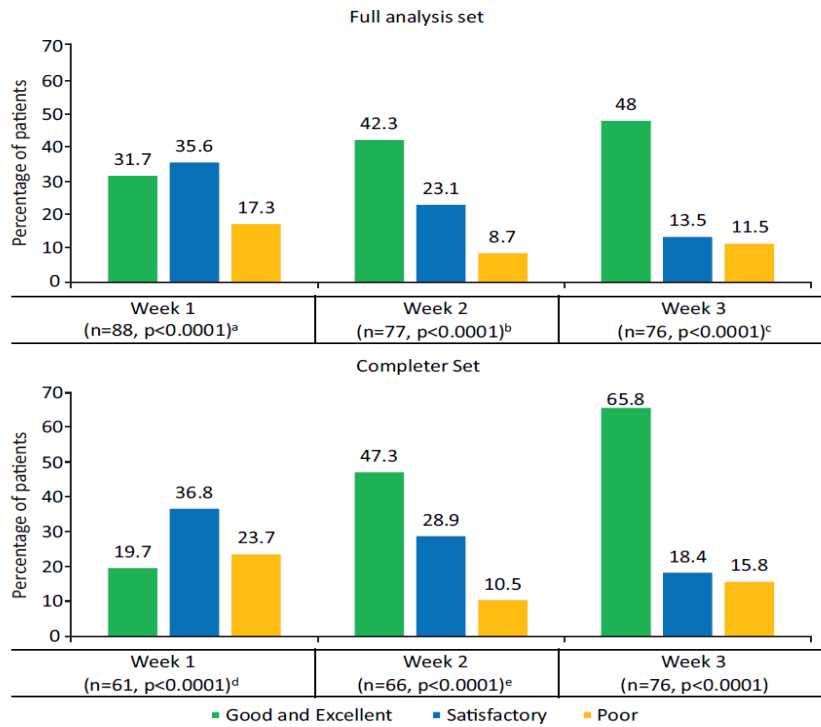


Figure 3: Physician's global assessment of effectiveness and safety.

^a15.4% of the patients missing at 1st week; ^b25.9% of the patients missing at 2nd week; ^c26.9% of the patients missing at 3rd week in FAS; ^d19.8% of the patients missing at 1st week; ^e13.3% of the patients missing at 2nd week.

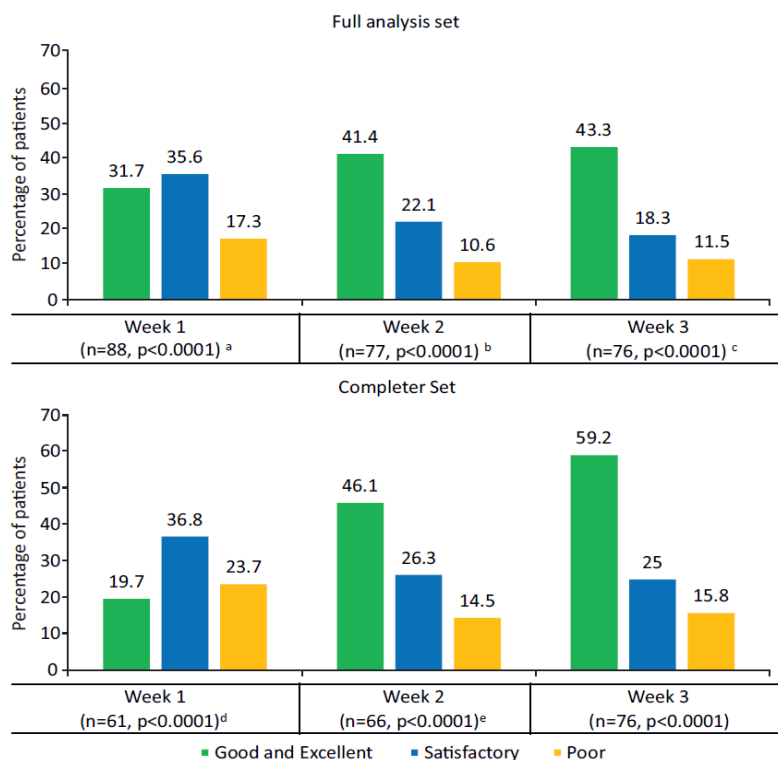


Figure 4: Patient's assessment of effectiveness and acceptability.

^a15.4% of the patients missing at 1st week; ^b25.9% of the patients missing at 2nd week; ^c26.9% of the patients missing at 3rd week in FAS; ^d19.8% of the patients missing at 1st week; ^e13.3% of the patients missing at 2nd week.

Safety

Of 104 patients evaluated in the safety assessment, only 1 (<1.0%) patient experienced fever of mild intensity,

which was resolved and considered nonserious (Table 4). The site investigator considered this AE as not related to study drug. Discontinuation due to adverse events were not observed in these patients.

Table 4: Summary of overall adverse events (safety population).

Summary of overall adverse events	Evaluable population (N=104)
Patients with overall AEs, N (%)	1 (<1.0)
Patients with serious AEs, N (%)	0
Patients with study product related AE's, N (%)	0
Patients with AEs by severity, N (%)	1 (<1.0)
Patients with AE's related to study treatment, N (%)	0
Patients with AE's unrelated to study treatment, N (%)	1 (<1.0)
Outcome, N (%)	
Completely recovered/resolved	1 (<1.0)

AE, adverse events

Table 5: Shift table- Summary of patients with sign and symptom scores from baseline to weeks of treatment (full analysis set).

Data collection	No. of patients (N)	Category	0	1	2	3
Assessment of erythema, N (%)						
Baseline	104		6 (5.8)	18 (17.3)	12 (11.5)	68 (65.4)
1st week	88	0	5 (4.8)	1 (1.0)	0 (0.0)	0 (0.0)
		1	4 (3.8)	12 (11.5)	2 (1.9)	0 (0.0)
		2	1 (1.0)	5 (4.8)	6 (5.8)	0 (0.0)
		3	1 (1.0)	6 (5.8)	31 (29.8)	14 (13.5)
2nd week	77	0	4 (3.8)	1 (1.0)	0 (0.0)	0 (0.0)
		1	6 (5.8)	6 (5.8)	0 (0.0)	1 (1.0)
		2	3 (2.9)	3 (2.9)	2 (1.9)	1 (1.0)
		3	1 (1.0)	20 (19.2)	24 (23.1)	5 (4.8)
3rd week	76	0	6 (5.8)	0 (0.0)	0 (0.0)	0 (0.0)
		1	7 (6.7)	3 (2.9)	0 (0.0)	0 (0.0)
		2	3 (2.9)	2 (1.9)	0 (0.0)	1 (1.0)
		3	15 (14.4)	24 (23.1)	13 (12.5)	2 (1.9)
Assessment of itching, N (%)						
Baseline	104		0 (0.0)	11 (10.6)	21 (20.2)	72 (69.2)
1st week	88	0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		1	1 (1.0)	4 (3.8)	2 (1.9)	0 (0.0)
		2	1 (1.0)	10 (9.6)	7 (6.7)	1 (1.0)
		3	5 (4.8)	11 (10.6)	28 (26.9)	18 (17.3)
2nd week	77	0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		1	4 (3.8)	2 (1.9)	0 (0.0)	1 (1.0)
		2	2 (1.9)	10 (9.6)	1 (1.0)	1 (1.0)
		3	5 (4.8)	22 (21.2)	20 (19.2)	9 (8.7)
3rd week	76	0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		1	5 (4.8)	1 (1.0)	1 (1.0)	0 (0.0)
		2	8 (7.7)	4 (3.8)	1 (1.0)	1 (1.0)
		3	17 (16.3)	19 (18.3)	10 (9.6)	9 (8.7)
Assessment of scaling, N (%)						
Baseline	104		2 (1.9)	25 (24.0)	39 (37.5)	38 (36.5)
1st week	88	0	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
		1	7 (6.7)	11 (10.6)	2 (1.9)	0 (0.0)
		2	3 (2.9)	15 (14.4)	13 (12.5)	1 (1.0)
		3	1 (1.0)	10 (9.6)	19 (18.3)	4 (3.8)

Continued.

Data collection	No. of patients (N)	Category	0	1	2	3
2nd week	77	0	2 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)
		1	10 (9.6)	5 (4.8)	2 (1.9)	0 (0.0)
		2	9 (8.7)	17 (16.3)	5 (4.8)	0 (0.0)
		3	1 (1.0)	18 (17.3)	8 (7.7)	0 (0.0)
3rd week	76	0	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
		1	16 (15.4)	0 (0.0)	1 (1.0)	0 (0.0)
		2	16 (15.4)	16 (15.4)	2 (1.9)	0 (0.0)
		3	10 (9.6)	14 (13.5)	0 (0.0)	0 (0.0)

Assessment of sign and symptom scores will be 0=Absent; 1=Mild; 2=Moderate; 3= Severe

DISCUSSION

In the last 5–6 years, an alarming rise in prevalence of dermatophytosis across India has been observed, with the highest prevalence of infections caused due to *T. rubrum*; however, recent studies also suggest increased prevalence of *T. mentagrophytes* infections causing inflammatory lesions in Indian patients.²²⁻²⁴ Fungal infections, especially in intertriginous areas, are often associated with inflammation and pruritus. Fungal infection due to inflammatory lesions causes erythema, itching and scaling and treating these individual symptoms efficiently is necessary for combating the infection.^{25,26} The first line of therapy for superficial, uncomplicated dermatophytes involves topical antifungal agents for their high efficacy and low adverse effects. These are available in various formulations such as creams, lotions, gels, or sprays for better permeation of fungal cell membrane and prolonged action. The efficacy of these drugs is facilitated by better penetration and convenience of application to the site of infection.²⁷

The in-vivo anti-inflammatory activity of Eberconazole can be attributed to the inhibition of 5-lipoxygenase and is specifically useful in conditions such as inflamed cutaneous mycoses, favoring the reduction in inflammatory symptoms and enhancing treatment compliance.²⁸ It has a broad spectrum anti-fungal and anti-inflammatory activity that could be effective in the treatment of cutaneous fungal conditions with pronounced inflammation. Eberconazole is currently marketed as a cream with a distinctive lipophilic-hydrophilic molecular structure which is to be applied on the skin surface of the infected region and spread by gentle massage to favor maximum absorption.²⁸

For the first time in real world setting, this Indian prospective, observational study in *Tinea corporis* and *Tinea cruris* infected patients treated with eberconazole 1% cream showed significant improvement in clinical outcomes. Substantial increase was observed in the proportion of patients with total signs and symptoms score of ≤ 2 at 2nd week from baseline suggesting a significant clinical improvement after treatment with eberconazole 1% cream. This improvement in total signs and symptoms score was noted within the 1st week of treatment. At least 50% of patients with scaling were completely relieved and erythema and itching subsided to

either mild intensity or was completely relieved by the end of 3rd week of treatment; similar to results observed in studies conducted by Shivamurthy et al and Lakhani et al. At 3rd week of treatment significant proportion of patients achieved total signs and symptoms score ≤ 2 , suggesting that appropriate treatment and patient compliance play a major role in good prognosis.^{10,29,30}

Eberconazole 1% cream was found to be extremely tolerable and safe for the treatment of *Tinea corporis* and *Tinea cruris* in the Indian population with only 1 AE (fever of mild intensity, unrelated to the study drug). The safety profile was consistent with other comparative study in Indian patients.²¹ Unlike other studies, local side effects such as erythema, stinging sensation, itching, or swelling were not observed in this study.^{13,19}

In a multicenter, double-blind, randomized clinical trial (RCT) in European patients with dermatophytes, 77% of the patients treated with eberconazole achieved effective response (sum of clinical signs and symptoms ≤ 2) within four weeks of continuous interventional treatment.¹⁸ In our study, over three weeks of treatment, approximately 55% of the patients achieved effective response and the improvement was significant at all evaluable timepoints. Another prospective, open-labelled, RCT conducted in 2018 with 75 Indian patients, reported eberconazole to be superior both in clinical improvement and fungal clearance and more effective in reducing pruritis and scaling when compared with luliconazole and sertaconazole. Similarly, in a phase 3 study by Montero et al, efficacy was assessed based on rate of effective response after four weeks through mycologic (mycological culture) and clinical (erythema, scaling, and itching) response where eberconazole 1% was found to be more effective than miconazole, ketoconazole and clotrimazole (76.1% for eberconazole and 75.0% with miconazole).¹⁸ In an open-label, comparative, RCT in Indian patients, global clinical assessment and patient’s assessment at the end of two weeks showed better response in eberconazole group (80% patients completely cured, 20% mild residual disease) compared with terbinafine group (80% with eberconazole 1% vs 63.3% with terbinafine). Clinical and mycological improvement with eberconazole were better at end of weeks 1 and 2.²¹

According to the in vitro susceptibility data, eberconazole was more active than the other three antifungal agents

(clotrimazole, miconazole, and ketoconazole) against the majority of the species tested. The minimum inhibitory concentration (MIC) of eberconazole was in range of 0.03 to 0.5 µg/mL for 31 isolates of *T. mentagrophytes* and 64 isolates of *T. rubrum*.³¹ Currently, topical terbinafine for a period of four weeks appears to be the treatment of choice for limited/localized disease.³² However, an increase in the MIC values of isolates to terbinafine were observed in various Indian studies.^{33,34} In other in vitro studies, eberconazole showed lowest MICs and was found to be more or equally active and thus could be a good alternative for the topical treatment of dermatophytosis.^{31,35}

According to a recent review on the current scenario of dermatophytosis in India, experts recommend usage of topical antifungal in treatment-naïve cases period. They also favored use of combination therapy or systemic antifungal therapy in patients with recalcitrant infections.¹⁶ For extensive infections, topical antifungal agents may also be used as an adjunct to oral antifungal therapy.^{14,32} Per the Cochrane review on topical antifungal treatment, systemic therapy is preferred in chronic and recalcitrant infections. Minimum duration for topical antifungals treatment should be once or twice daily for two to four weeks in treatment-naïve cases and >4 weeks in recalcitrant cases.³⁶ Experts have also advised continuing topical antifungal agents or systemic antifungal therapy for two weeks post clinical cure.¹⁶

There were a few limitations to this study. Due to the observational, real-world design, the response rates and compliance to all scheduled follow-up visits were lesser than those observed in interventional clinical trials with set duration of treatment. Long term follow-up was necessary when considering the therapeutic effects as recurrence is big problem for real world treatment in dermatomycosis. The current study did not compare eberconazole with the other topical antifungals however, some existing evidence favors eberconazole.^{18,19,21,37} There might be a confounding effect for patients who were on systemic antihistamine or other drugs. Mycological cure could not be evaluated as mycological assessments were not performed in routine clinical practice in any evaluable patient.

Eberconazole 1% cream for the treatment of *Tinea cruris* and *tinea corporis* can be effectively and safely used for the management of dermatophytoses in Indian patients with consideration for above described limitations.

CONCLUSION

The results of this real-world, prospective, observational study provide evidence for eberconazole 1% cream as an effective and tolerable treatment in the management of *Tinea cruris* and *tinea corporis* in Indian patients. Patients who completed at least three weeks of treatment showed optimal response. This study provides a valuable reflection of daily clinical practice especially in Indian

scenario, where limited RWE on topical antifungals exist. Hence the result will be useful to healthcare professionals in decision making and choosing an appropriate choice of treatment. Further studies with a larger sample size and appropriate comparative studies are required to support these findings.

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