

Comparative evaluation of Clotrimazole versus Sertaconazole in the treatment of tinea corporis

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Abstract

Background: Tinea corporis is a common dermatophytic infection affecting 22-25% of the world population. Clotrimazole is conventional antifungal drug whereas sertaconazole is newer antifungal claimed to be superior to clotrimazole. Both are used topically. **Aims and Objective:** To compare the efficacy and safety of topical clotrimazole versus sertaconazole in tinea corporis/cruris. **Materials and Methods:** A total of 60 patients diagnosed with tinea corporis/cruris were randomized into two groups of 30 patients each. Group A received topical clotrimazole (1% cream), and Group B received topical sertaconazole (2% cream). The patients were advised to apply the drug on affected area twice daily for 4 weeks. Outcome parameters such as pruritus, erythema, vesicles and desquamation, and potassium hydroxide mount were noted weekly for the assessment of efficacy. **Results:** There was significant reduction in pruritus ($P < 0.001$), erythema ($P < 0.001$), vesicles ($P < 0.001$), and desquamation ($P < 0.001$) among both the groups. The mean difference and the standard deviation of the total score of all parameters (baseline to 4th week follow-up) for clotrimazole group were 6.39 ± 1.123 and for sertaconazole group were 7.37 ± 0.751 , respectively. The P value on the application of students unpaired t -test was $P = 0.115$ (not significant). No serious adverse drug events in both the groups. **Conclusion:** Clotrimazole is as efficacious and safe as compared with sertaconazole in the treatment of tinea corporis/cruris. However, sertaconazole group has showed an early response to therapy compared to clotrimazole group.

Key words: Sertaconazole, Clotrimazole, Tinea Corporis/Cruris, Potassium Hydroxide.

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Introduction

Superficial fungal infections affects 20-25% of the population globally. The most common fungal infection includes Dermatophytoses. [1] This is a serious health problem in the hot and humid climate of tropical countries like India.[2] Clinically Tinea corporis and tinea cruris are the most common types dermatophytoses in India.[3] Though the dermatophytoses are not cause of mortality; but it causes morbidity and thereby affecting

the quality of life, poses hindrance in daily activities, and costs burden to health-care expenditure. The treatment protocol to treat dermatophytoses includes administration of either or both systemic or topical antifungal agent. Owing to the associated disadvantages of oral antifungal agent, the topical therapy is always preferred and has better compliance. [4-6] . For more than two decades, Clotrimazole has remained drug of choice for the treatment of the tinea corporis and cruris. The long duration of therapy with Clotrimazole sometimes is the reason for non-compliance or poor-compliance which results in high relapse rate and rapid development of resistance.[7-9] To overcome the pathogenicity of superficial fungal infections, development of newer broad-spectrum antifungals was much awaited. Drugs like sertaconazole have emerged as a new treatment options. Benzothioephene imidazole

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antifungal (topical Sertaconazole) is proved to be more efficacious compared to conventional azoles. This necessitates a shorter duration of treatment and has shown to have lower relapse rates.[3,10] Sertaconazole have dual action (fungistatic and fungicidal activity) against dermatophytes.[11-13] In addition, this also endows with anti-inflammatory action relieving itching that help to grant better symptomatic relief.[14,15] The additive action of sertaconazole is most likely to make an impact simultaneously on the symptomatic relief and therefore improving the quality of life of the patients affected with dermatophytoses.[16,17] To our knowledge, reported literature comparing efficacy, safety and cost-effectiveness of topical antifungals clotrimazole and sertaconazole in the treatment of tinea corporis/cruris are sparse. Hence, this study was conducted to compare the efficacy and safety of clotrimazole and sertaconazole for the treatment of tinea corporis/cruris.

Materials and methods

Study Design

This was a single-center, prospective, randomized, open-label, and comparative study. The study was conducted at Outpatient Department of Dermatology, at Vardhman Institute of Medical Sciences, Pawapuri.

Table 1: Symptoms and signs of pruritus, erythema, vesicles, and desquamation

0	Nil
1	Mild
2	Moderate
3	Severe

Patients were eligible for the study if they had a combined score of at least 5.

Drug Administration

Group 1 was treated with Clotrimazole 1% topical cream and the Group 2 received Sertaconazole 2% topical cream. It was advised to apply the test medication twice on affected area. The study was conducted over a total duration of 4 weeks. Patient's demographic data including age, sex, baseline clinical parameters such as pruritus, erythema, vesicles, and desquamation were noted at base line. All patients were followed one at 1st week, 2nd week, and 4th week. Outcome of the treatment was assessed.

Efficacy and Safety Assessments

The subjects were evaluated for the signs and symptoms viz; pruritus, erythema, vesicles, and desquamation. The signs and symptoms were graded as nil (0), mild (1), moderate (2), and severe (3). The primary efficacy parameter was change in the score of signs and symptoms for the affected area. The

The study was approved by Institutional Research Committee. An informed and written consent was obtained from all the participating subjects enrolled in the study. The study sample included patients with clinical evidence of tinea corporis/cruris and was confirmed with skin scraping positive for potassium hydroxide (KOH) mount.

Randomization

The estimated sample size for the study was 60 subjects divided into two groups (30 in each group). Patients who fulfilled the eligibility criteria were randomly divided into two treatment groups (1:1 ratio).

Inclusion Criteria

The criteria for inclusion in the study were:-

1. Patients of both genders in age group of 18-65 years.
2. Clinical manifestations of cutaneous mycoses (tinea corporis/cruris).

Exclusion criteria

The criteria for exclusion in the study were:-

1. Pregnant and Lactating mothers,
2. Systemic Disease
3. Hypersensitivity toazole drugs or vehicle ingredients,
4. Previous treatment with antifungal, antibiotic or immunosuppressant agents.

Symptoms and signs were scored as shown in the table 1.

secondary efficacy result was mycological cure based on KOH test: A negative KOH preparation at the end of the study period was considered as mycological cure. The change in total score was also assessed. The safety of study medication was assessed in all patients by recording adverse drug reactions (ADRs) as reported by them. The details of occurrence, intensity and causal relationship to the study drug along with the findings of physical and clinical examination were considered.

Statistical Analysis

The data was tabulated in Microsoft excel. Descriptive statistics were reported for continuous parametric variables. Statistical analysis was performed using SPSS Software version 11.0. Differences in clinical score within group were compared by one-way analysis of variance. Unpaired t-test was employed to find the significance in between the group. A difference was considered as significant if the $P < 0.05$.

Results

Study Profile and Baseline Characteristics

Out of 60 patients participated in the study (30 in each group), only 56 patients completed the trial. A total of 4 patients comprising of 1 and 3 from clotrimazole

group and sertaconazole group respectively were lost to follow-up. The demographic and baseline clinical characteristics of study patients is presented in Table 2.

Table 2: Baseline demographic and clinical characteristics of patients.

Characteristic	Clotrimazole	Sertaconazole
Number of patients	30	30
Number of patients completed trial	29	27
Age (years) (mean±SD)	32.26±11.16	30.76±10.35
Male	19	18
Female	11	12
Tinea corporis	20	18
Tinea cruris	10	12

Efficacy Parameters

Both groups of patients showed a significant reduction in pruritus, erythema, vesicles, and desquamation from baseline across time at the end of 4 weeks ($P < 0.001$). There was a faster reduction in mean scores of pruritus, erythema, and desquamation by sertaconazole ($P < 0.001$) compared to clotrimazole ($P < 0.01$) from baseline to 1st week (first follow-up) and reduction in

vesicle was comparable in both groups ($P < 0.01$). However, no significant difference was found when 2nd week was compared to 4th week in both treatment groups (Table 3). The reduction in total score by sertaconazole was steep and faster compared to clotrimazole from baseline to 4th week as presented in Table 3.

Table 3: Intragroup comparison of mean scores of primary efficacy parameters at 1st week, 2nd week, and 4th week

Parameter	Baseline	1 st week	2 nd week	4 th week
Clotrimazole				
Pruritis	2.73±0.80	2.06±0.57*	1.73±0.69***	1.43±0.56***
Erythema	2.63±0.71	1.8±0.71**	1.23±0.5***	0.6±0.49***
Vesicles	1.36±1.12	0.66±0.71**	0.23±0.43***	0***
Desquamation	1.9±0.99	1.16±0.83**	0.46±0.57**	0.2±0.4***
Sertaconazole				
Pruritis	2.70±0.66	1.73±0.77***	1.46±0.75***	1.26±0.63***
Erythema	2.6±1.27	1.6±1.16***	0.9±0.75***	0.3±0.46***
Vesicles	1.73±1.2	0.73±0.9**	0.1±0.3***	0***
Desquamation	2.13±0.93	1.06±0.86***	0.63±0.8***	0.23±0.43***

All values are expressed in mean±SD. One-way ANOVA was used. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, SD: Standard deviation, ANOVA: Analysis of variance

Table 4 shows the intergroup comparison of mean difference of pruritus, erythema, vesicles, and desquamation scores at 1st week, 2nd week, and 4th week from the baseline score in both treatment groups. Symptoms of pruritus and desquamation have shown a statistically significant reduction ($P < 0.05$) in sertaconazole group when compared with clotrimazole group at the end of 1st week. There was no statistically significant difference in reduction in the scores of erythema and vesicles in between the groups. The

mean difference of baseline to 2nd week's score was highly significant ($P < 0.01$) in pruritus, significant ($P < 0.05$) in vesicles and nonsignificant in erythema and desquamation when sertaconazole 2% cream was compared with clotrimazole 1% cream. However, mean difference of the baseline to 4th week's score was statistically significant only for pruritus, but nonsignificant for erythema, vesicles and desquamation score when the two group drugs were compared.

Table 4: Intergroup comparison of mean differences in scores of signs and symptoms at 1st, 2nd, and 4th week from baseline score

Duration Parameters	Baseline to 1 st week		Baseline to 2 nd week		Baseline to 4 th week	
	Clotrimazole	Sertaconazole	Clotrimazole	Sertaconazole	Clotrimazole	Sertaconazole
Pruritis	0.67±0.23	0.97±0.21*	1±0.25	1.24±0.22*	1.3±0.22	1.44±0.26**
Erythema	0.83±0.17	1±0.21	1.4±0.27	1.7±0.28	2.03±0.26	2.3±0.4
Vesicles	0.7±0.28	1±0.27	1.13±0.35	1.63±0.42*	1.36±0.42	1.73±0.44
Desquamation	0.73±0.21	1.07±0.19*	1.43±0.32	1.5±0.27	1.7±0.34	1.9±0.31

All values are expressed in mean±SD. Unpaired *t*-test was used. **P*<0.05 and ***P*<0.01, SD: Standard deviation

Safety Parameters

Both drug treatments were well-tolerated. However, two patients complained of burning with clotrimazole and redness was reported in one patient with sertaconazole. All three ADRs were mild, self-limiting, and did not require the discontinuation of therapy.

Discussion

Dermatophytes invade the keratinized tissue (skin, hair, and nails) and belongs to taxonomically related fungi.[4] This disease common in most tropical countries including India. In the last four to five decades incidence of tinea infections has increased progressively. The increasing population of immunocompromised individuals is the reason for it. [18] Azole group antifungal agents (Clotrimazole) are the most commonly used broad-spectrum topical antifungal agent.[7,9] Sertaconazole is a newer antifungal agent belonging to benzothiazophene imidazole. Sertaconazole is found to be more effective than azoles in several studies.[3,10] The present study, compared the efficacy clotrimazole 1% cream and sertaconazole 2% cream for the patients suffering from mild to moderate tinea corporis/cruris. The drug was applied twice daily for 4 weeks on the affected area. There was a significant reduction in symptoms and signs viz; pruritus, erythema, vesicles, and desquamation as noted on baseline in both the study groups. However, sertaconazole group showed fast response to therapy compared to clotrimazole group. A similar results was reported in studies of Khan et al.,[3] Shivamurthy et al.,[7] and Jerajani et al.[10] An apparent reason for this may be credited to its wide range of action. This has dual action of both fungistatic and fungicidal activity. Its fungistatic action is due to inhibition of fungal cell wall synthesis caused by non conversion of lanosterol to ergosterol. At high concentrations sertaconazole causes cell death by binding directly to non-sterol lipids on the fungal membrane.[11-13] The current study also found

sertaconazole group highly significantly reducing pruritus compared to clotrimazole group, which shows early response. This gives explanation for the anti-inflammatory action of sertaconazole. This is mediated by reducing release of inflammatory mediators and release of prostaglandin E2, these mechanisms control the inflammatory pathway of dermatophytosis. [14,15] This study also showed a mycologically negative percentage of sertaconazole 2% cream to be greater than clotrimazole 1% cream. The mycologically negative with KOH mount at the end of 2nd week was 93% for patients treated with sertaconazole 2% cream and 58% patients for clotrimazole 1% cream. Though both the groups had absolute mycological cure (100%) at the conclusion of 4th week, but sertaconazole group shown an early mycological cure compared to clotrimazole. This was in consonance with the study reports of Khan et al., wherein, sertaconazole 2% cream (94%) was superior to clotrimazole 1% cream (62%) in early mycological cure, but both were equally effective in mycological assessment at the end of study. [3] Shivamurthy et al. found no significance difference between sertaconazole and clotrimazole creams on KOH mount.[7] A total of three adverse drug reactions were reported in this study. Two patients reported burning sensation with clotrimazole, and one patient reported redness with sertaconazole. All these three complaints were mild and did not required discontinuation of therapy. This is in consistent with the previous study of Khan et al., where only one patient in sertaconazole group reported burning sensation. [3] On the other hand Sharma et al., reported five subjects with mild to moderate adverse events in the sertaconazole group.[19]

Conclusion

The results of this study indicate that symptoms and signs of tinea corporis/cruris are relieved earlier and better with sertaconazole compared to clotrimazole. But both medications were equally efficacious in

mycological cure at the end of 4th week. Therefore, sertaconazole 2% cream can be the preferred choice as first-line agent followed by clotrimazole 2% cream. However, the cost effectiveness of clotrimazole must also be considered.

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