

## Comparative Assessment of the Efficacy of Three Different Topical Anti-Fungal Drugs in the Management of Tinea Corporis and Tinea Cruris

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Conflict of interest: Nil

### Abstract

**Aim:** The aim of the present study was to assess the efficacy of topical amorolfine, luliconazole, sertaconazole, terbinafine in tinea corporis and tinea cruris.

**Methods:** This was a prospective, randomized study was done in the Department of skin and VD, Jai Prakash Narayan Hospital, Gaya, Bihar, India for six months . It was a pragmatic study to assess the therapeutic response to certain topical antifungals in the current scenario of dermatophytosis. Total 200 clinically diagnosed healthy adult patients with tinea corporis and tinea cruris requiring topical antifungal therapy were include in this study.

**Results:** Among 200 patients 90 were treatment naive, 50 were topical steroid (with or without antifungal) modified cases, 48 were partially treated with antifungals and 12 had used home remedies prior to the study. Luliconazole showed best improvement of pruritus (mean-1.45), erythema (mean-1.42) and scaling (mean- 1.49). Terbinafine showed the least improvement with mean being 0.64, 0.55, 0.73 for pruritis, erythema and scaling respectively. Difference in the mean values of improvement of luliconazole as compared to the other three drugs was significant for pruritus and highly significant for erythema and scaling. Total value of improvement in pruritus, erythema and scaling were calculated and patients were grouped into poor response (total score- 0, 1 & 2), moderate response (total score-3&4) and good response (total score-5&6). A total of 30 patients (60%) in luliconazole group showed good response as compared to the other drugs. These differences in the improvement of patients were statistically significant as compared to other drugs.

**Conclusion:** We concluded that the Luliconazole may score over other 3 topical antifungals. Although it belongs to azole class, it seems to exhibits fungicidal activity. This study also signifies the role of topical antifungal alone in treating limited tinea corporis and cruris, thus boosting the confidence on topical therapy. Newer topical antifungals are more expensive and hence pharmaco-economical analysis should also be considered while prescribing them.

**Keywords:** Dermatophytoses, luliconazole, sertaconazole, terbinafine, tinea corporis, tinea cruri

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### Introduction

Dermatophytes are a group of taxonomically related fungi. [1] The disease is caused by dermatophytes

belonging to genera of Trichophyton, Microsporum and Epidermatophyton. The fungal infections of the skin and its

appendages are more common in tropical countries like India due to environmental factors like heat (summer) and humidity (monsoon). The risk factors include socio-economic conditions like overcrowding and poverty leading to poor personal hygiene. The type and frequency of dermatophytoses may change with time, due to changes in living standards and application of preventive measures like personal hygiene. However in India, the most commonly occurring clinical type of dermatophytoses for adults includes, tinea corporis (36-59%) and tinea cruris (12-27%). [2,3]

Sertaconazole is a new benzothioephene imidazole derivative that is being used worldwide for varied indications including dermatophytosis, candidiasis, pityriasis versicolor, seborrhoeic dermatitis of scalp. Sertaconazole has both fungi static and fungicidal activity against Dermatophytes, *Candida* spp. and *Cryptococcus* fungal infections. It is also effective against *Aspergillus* fungi and Gram-positive bacteria (*Staphylococcus* and *Streptococcus* genera), that are likely to cause secondary infections. [4,5] This action is attributable to its indirect inhibition of ergosterol synthesis and direct inhibition of nonsterol component of fungal cell membrane leading to rapid leakage of key intracellular components and immediate cell death. Additionally, the unique benzothioephene ring in the chemical structure offers higher lipophilicity and greater retention of drug in the stratum corneum) for up to 48 hrs, leads to greater mycological cure rates and lesser chance of relapse. [6] The anti-inflammatory and anti-pruritic actions of Sertaconazole leads to symptomatic relief and is considered to be beneficial to patients. [7-9] These ancillary properties of sertaconazole are likely to make an impact on the concomitant symptom control and therefore improve quality of life of these patients with dermatophytoses. Drug resistance is a common problem with most

of the antifungal agents; however the data for sertaconazole is quite limited. According to resistance testing conducted in European settings, 4% strains were resistant to sertaconazole compared to 48.8% with triazoles (fluconazole). [10] Sertaconazole has excellent safety record, with the reported adverse event being cutaneous related including contact dermatitis, dryness, burning, eczema, itching and skin tenderness. However the frequency of these side effects was comparable to placebo. [11]

Within the past few years, new extended-spectrum triazoles and allylamines have been introduced into market among such are Luliconazole, Sertaconazole, Eberconazole which belong to triazoles and Amorolfine which belong to Allyamine group. Dermatophytes constitutes a group of about 40 fungal species that are members of the Trichophyton, Microsporium, and Epidermophyton genere and cause superficial infection called dermatophytosis, ringworm, or tinea. [12,13] The aim of the present study was to assess the efficacy of topical amorolfine, luliconazole, sertaconazole, terbinafine in tinea corporis and tinea cruris.

### Materials and Methods

This was a prospective, randomized study was done in the Department of skin and VD, Jai Prakash Narayan Hospital, Gaya, Bihar, India for six months . It was a pragmatic study to assess the therapeutic response to certain topical antifungals in the current scenario of dermatophytosis. Total 200 clinically diagnosed healthy adult patients with tinea corporis and tinea cruris requiring topical antifungal therapy were include in this study. Recurrent, steroid modified and partly treated tinea infections were also recruited in order to represent the current scenario. A detailed history including the duration of disease, associated medical conditions, treatment history and family history were taken. An

arbitrary sample size of 100 was considered with 50 patients in each category of antifungal was considered.

Location of lesion, morphology and symptoms were noted. Scrapings from the edge and/or from the scaly area of the lesions were taken. Potassium hydroxide mount (KOH Mount) followed by direct microscopy was undertaken at the beginning of treatment to confirm the diagnosis but not repeated at the end of treatment since clinical improvement rather than a cure was the primary objective of the study. Consecutive eligible patients were prescribed topical amorolfine (0.25%), luliconazole (1%), sertaconazole (2%) and terbinafine (1%) in a serial order. Amorolfine and luliconazole were advised

once daily while sertaconazole and terbinafine was twice daily application. They were asked to apply as a thin layer directly to the lesions and also a small area beyond the lesions. Response to treatment was assessed after 3 weeks with no follow-up visit.

We evaluated the improvement in the pruritus, erythema and scaling with score 0 for no improvement, score 1 for partial improvement and score 2 for complete improvement. Therapeutic response was statistically evaluated using Kruskal Wallis test and Fishers exact test. Antihistamine tablet levocetirizine 5 mg at bed time was given for 7 days to all patients as an anti-pruritic medication.

### Results

**Table 1: Previous topical treatment**

| Group         | Naive | Steroid | Antifungal | Others | Total |
|---------------|-------|---------|------------|--------|-------|
| Amorolfine    | 12    | 23      | 12         | 3      | 50    |
| Luliconazole  | 28    | 4       | 14         | 4      | 50    |
| Sertaconazole | 26    | 12      | 10         | 2      | 50    |
| Terbinafine   | 24    | 11      | 12         | 3      | 50    |
| Total         | 90    | 50      | 48         | 12     | 200   |

Among 200 patients 90 were treatment naive, 50 were topical steroid (with or without antifungal) modified cases, 48 were partially treated with antifungals and 12 had used home remedies prior to the study.

**Table 2: Comparison between pruritus, erythema & scaling**

| Parameters | Group         | N  | Mean | P value |
|------------|---------------|----|------|---------|
| Pruritus   | Amorolfine    | 50 | 1.15 | .012    |
|            | Luliconazole  | 50 | 1.45 |         |
|            | Sertaconazole | 50 | 1.36 |         |
|            | Terbinafine   | 50 | 0.64 |         |
| Erythema   | Amorolfine    | 50 | 0.96 | .002    |
|            | Luliconazole  | 50 | 1.42 |         |
|            | Sertaconazole | 50 | 1.04 |         |
|            | Terbinafine   | 50 | 0.55 |         |
| Scaling    | Amorolfine    | 50 | 0.95 | .004    |
|            | Luliconazole  | 50 | 1.49 |         |
|            | Sertaconazole | 50 | 1.15 |         |
|            | Terbinafine   | 50 | 0.73 |         |
| Total      | Amorolfine    | 50 | 2.55 | .003    |
|            | Luliconazole  | 50 | 4.75 |         |
|            | Sertaconazole | 50 | 3.65 |         |
|            | Terbinafine   | 50 | 2.28 |         |

Luliconazole showed best improvement of pruritus (mean-1.45), erythema (mean-1.42) and scaling (mean- 1.49). Terbinafine showed the least improvement with mean being 0.64, 0.55, 0.73 for pruritis, erythema and scaling respectively.

Difference in the mean values of improvement of luliconazole as compared to the other three drugs was significant for pruritus and highly significant for erythema and scaling.

**Table 3: Group comparison of drugs**

| Response | Amorolfine |     | Luliconazole |     | Sertaconazole |     | Terbinafine |     |
|----------|------------|-----|--------------|-----|---------------|-----|-------------|-----|
|          | N=50       | %   | N=50         | %   | N=50          | %   | N=50        | %   |
| Poor     | 21         | 42  | 5            | 10  | 12            | 24  | 24          | 48  |
| Moderate | 19         | 38  | 15           | 30  | 22            | 44  | 24          | 48  |
| Good     | 10         | 20  | 30           | 60  | 16            | 32  | 2           | 4   |
| Total    | 50         | 100 | 50           | 100 | 50            | 100 | 50          | 100 |

Total value of improvement in pruritus, erythema and scaling were calculated and patients were grouped into poor response (total score- 0, 1 & 2), moderate response (total score-3&4) and good response (total score-5&6). A total of 30 patients (60%) in luliconazole group showed good response as compared to the other drugs. These differences in the improvement of patients were statistically significant as compared to other drugs.

### Discussion

Dermatophytosis is commonly designated as tinea, is caused by keratinophilic fungi called as dermatophytes. Infection is generally limited to the superficial layers of the epidermis, particularly the stratum corneum and the high keratin concentration containing appendageal structures, namely hair and nails. Dermatophytes are classified in three genera- Epidermophyton, Trichophyton and Microsporum. Tinea corporis and tinea cruris refer to the dermatophytic infections of the glabrous skin of the body (excluding palms and soles) and groins respectively. Topical antifungals are exclusively used for localized lesions of dermatophytosis.

Amorolfine, luliconazole, sertaconazole and terbinafine are relatively newer molecules which seem to have certain advantages over the older molecules. Topical daily antifungal therapy is considered generally as the first

line therapy for dermatophytosis owing to their high efficacy and low potential for side effects. Terbinafine is a fungicidal allylamine that inhibits squalene epoxidase that results in intracellular accumulation of toxic squalene and causes fungal cell death. Luliconazole and sertaconazole are azoles antifungals that block lanosterol 14- $\alpha$  demethylase which prevents the formation of ergosterol. [14]

This substantiates the antipruritic and anti-inflammatory action of sertaconazole over other antifungals that would ensure better adherence to treatment and improved quality of life. This antipruritic and anti-inflammatory property of sertaconazole is due to its ability to reduce histamine release and several other proinflammatory cytokines including PGE2. The clinical implication of this is significant since for most patients with tinea infections topical imidazoles are usually advocated where sertaconazole shows highest antimycotic potency compared to other antifungal agents especially against candida albicans that are also likely to be involved or concomitantly present in a patient of tinea cruris. [9,15]

Luliconazole showed best improvement of pruritus (mean-1.45), erythema (mean-1.42) and scaling (mean- 1.49). Terbinafine showed the least improvement with mean being 0.64, 0.55, 0.73 for pruritis, erythema and scaling respectively.

Difference in the mean values of improvement of luliconazole as compared to the other three drugs was significant for pruritus and highly significant for erythema and scaling. Jerajani et al conducted almost a similar study and found sertaconazole exhibiting better response than luliconazole and terbinafine. [16] Another study conducted by Choudhary et al showed equal efficacy between sertaconazole and terbinafine. [17] Total value of improvement in pruritus, erythema and scaling were calculated and patients were grouped into poor response (total score- 0, 1 & 2), moderate response (total score-3&4) and good response (total score-5&6). A total of 30 patients (60%) in luliconazole group showed good response as compared to the other drugs. These differences in the improvement of patients were statistically significant as compared to other drugs. There seem to be a poor response to the fungicidal drug terbinafine which could be due to various factors that may include drug resistance. [18]

### Conclusion

We concluded that the Luliconazole may score over other 3 topical antifungals. Although it belongs to azole class, it seems to exhibit fungicidal activity. This study also signifies the role of topical antifungal alone in treating limited tinea corporis and cruris, thus boosting the confidence on topical therapy. Newer topical antifungals are more expensive and hence pharmacoeconomical analysis should also be considered while prescribing them.

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