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Original Research

Comparative evaluation of efficacy and safety of topical Luliconazole and Amorolifine in the treatment of tinea corporis

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***ABSTRACT*:**
Background: Fungal infection of skin is a significant public health problem. They are caused by three genera of dermatophytes; Trichophyton, Microsporum and Epidermophyton. The present study was a comparative evaluation of efficacy and safety of topical luliconazole and amorolifine in the treatment of tinea corporis. **Materials & Methods:** The present study was conducted on 70 patients. Group I patients received topical application of Luliconazole (1%) and Group II patients received topical application of Amorolfine (0.25%). Clinical examination was done on all patients for determining the number of lesion, type, presence of inflammatory margins and extent of involvement. Size of lesion, margin of the lesion, erythema, scaling and itching was noted. Mycological examination was also done with KOH mount**.** Baseline score (Day 0) was assessed before applying topical medication. Post treatment scores on all parameters were taken on day 7, 14, 21, and 28. **Results:** Out of 70 patients, males were 40 and females were 30. There was significant difference in size of lesion in all days ($P< 0.05$). There was significant difference in size of lesion in all days ($P< 0.05$). **Conclusion:** Authors found that both 1% Luliconazole and 0.25% Amorolifine were effective in management of tinea corporis.
Key words: Dermatophytes, Trichophyton, Microsporum

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INTRODUCTION

These dermatophytes need essentially the keratin for their growth and remain restricted to hair, nails and superficial skin. This characteristic underscores the importance of treatment with topical antifungal medications.[2]

Tinea corporis (ringworm) typically presents as a red, annular, scaly, pruritic patch with central clearing and an active border. Lesions may be single or multiple and the size generally ranges from 1 to 5 cm, but larger lesions and confluence of lesions can also occur. Tinea corporis may be mistaken for many other skin disorders, especially eczema, psoriasis, and seborrheic dermatitis.[3]

A potassium hydroxide (KOH) preparation is often helpful when the diagnosis is uncertain based on history and visual inspection. Worsening after empiric treatment with a topical steroid should raise the suspicion of a dermatophyte infection. Conversely, if a nonfungal lesion is treated with an antifungal cream, the lesion will likely not improve or will worsen. Cultures are usually not necessary to diagnose tinea corporis. Skin biopsy with periodic acid–Schiff (PAS) stain may rarely be indicated for atypical or persistent lesions.[4] The present study was a comparative evaluation of efficacy and safety of topical

luliconazole and amorolifine in the treatment of tinea corporis.

MATERIALS & METHODS

The present prospective, randomized, open label, intention to treat, comparative study was conducted in Department of Pharmacology, GMC Jammu in collaboration with Department of Dermatology, SMGS Hospital, Jammu, a tertiary care teaching hospital over a period of one year. Inclusion criteria was newly diagnosed OPD patients of either sex between the ages of 18 to 50 years with tinea corporis. With atleast two of the three major clinical manifestations of tinea (Erythema, Scaling and Itching) and single or multiple lesion limited to one site of the body with area involved less than 30cm in major dimensions and mycological conformation (positive KOH test) for tinea corporis. Exclusion criteria was patients with systemic mycosis /tinea involving more than one body region simultaneously, patients with pre-treatment with any topical or oral antifungal drugs / immunosuppressant drugs etc.

Patients were divided into two groups comprised of 35 patients in each. Group I patients received topical application of Luliconazole (1%) and Group II patients received topical application of Amorolfine (0.25%).

Detailed history for demographic features and clinical examination in good light was done on all patients for determining the number of lesion, type, presence of inflammatory margins and extent of involvement. Size of lesion, margin of the lesion, erythema, scaling and itching was noted. Mycological examination was also done with KOH mount**.** Baseline score (Day 0) was assessed before applying topical medication (Fig- 1). Post treatment scores on all parameters were taken on day 7, 14, 21, and 28 (Fig- 2).

RESULTS

Table I Distribution of patients

Total- 70		
Gender	**Males**	**Females**
Number	40	30

Table I shows that out of 70 patients, males were 40 and females were 30.

Table II Improvement in Size of Skin Lesion in Group I Luliconazole (1%) Patients

Day	**Size of Skin Lesion (cm)**				
	<1 No. (%)	**1-5 No. (%)**	**5-10 No. (%)**	**10-20 No. (%)**	**>20 No. (%)**
0	0	5 (14.28)	18 (51.43)	7 (20.00)	5 (14.28)
7	0	7 (20.00)	16 (45.71)	7 (20.00)	5 (14.28)
14	0	17 (48.57)	12 (34.28)	6 (17.14)	0
21	0	23 (65.71)	7 (20.00)	5 (14.28)	0
28	1 (2.86)	24 (68.57)	9 (25.71)	1 (2.86)	0
Statistical Inference (Fisher's Exact Test)	***p=1.00****	***p<0.0001****	***P=0.04****	***p=0.05****	***p=0.05****

Table II shows that there was significant difference in size of lesion in all days (P< 0.05).

Table III Improvement in Size of Skin Lesion in Group II Amorolifine (0.25%) Patients

Day	Size of Skin Lesion (cm)				
	<1 No. (%)	**1-5 No. (%)**	**5-10 No. (%)**	**10-20 No. (%)**	**>20 No. (%)**
0	0	2 (5.71)	22 (62.86)	11 (31.43)	0
7	0	2 (5.71)	23 (65.71)	10 (28.57)	0
14	1 (2.86)	10 (28.57)	21 (60.00)	3 (8.57)	0
21	1 (2.86)	20 (57.15)	11 (31.43)	3 (8.57)	0
28	1 (2.86)	23 (65.71)	9 (25.71)	2 (5.71)	0
Statistical Inference (Fisher's Exact Test)	**p=1.00***	**p<0.0001****	**P=0.003****	**p=0.01****	**-**

Table III shows that there was significant difference in size of lesion in all days (P< 0.05).

Table IV Comparative effect of Luliconazole (1%) and Amorolifine (0.25%) on Size of Skin lesion

Day	Group A (n = 35) Mean ± SD	Group B (n = 35) Mean ± SD	T	p
Day 0	2.34 ± 0.90	2.25 ± 0.56	0.502	0.617
Day 7	2.28 ± 0.95	2.22 ± 0.54	0.325	0.746
Day 14	1.68 ± 0.75	1.74 ± 0.65	0.358	0.722
Day 21	1.48 ± 0.74	1.45 ± 0.70	0.174	0.862
Day 28	1.28 ± 0.57	1.34 ± 0.63	0.418	0.677

Table IV shows non- significant intergroup difference in size of lesion.

DISCUSSION:

Mycoses is characterized as superficial, subcutaneous and deep. In superficial the fungal infection involves stratum corneum, hair and nails. Subcutaneous involves dermis and subcutaneous tissue while deeper systemic mycoses represent haematogenous spread of organism in immune compromised or critically ill patient. Deep or systemic fungal infection is important cause of hospitalization or mortality, while the other two are managed on OPD basis. Dermatophytes cause superficial fungal infections. Tinea corporis signifies tinea infection anywhere in the body except tinea capitis (scalp), tinea barbae (beard), tinea pedis (feet) or tinea mannum (hands).[5]

Fungal infections are persistent and not easily cleared by the handful of drugs currently available and as a result, the infections often reoccur. Fungi are eukaryotes unlike bacteria which are prokaryotes and as such they respond to antibiotics without harming normal human cells. Treatment of tinea consists of antifungal drugs or chemotherapeutic agents which act directly or indirectly on the fungi to eradicate the infection. Antifungals are broadly classified as Polyenes (Nystatin, Amphotericin B), Azole derivatives (Imidazole, Ketoconazole, Clotrimazole, Sertaconazole, Fluconazole etc), Allylamine (Terbinafine, Butenafine etc), Equinocandines (Caspofungin, Micafungin), Hydropyridone (Cyclopirox), Morpholine derivatives (Amorolfine) while others include Griseofulvin.[6]

Imidazoline derivatives with antifungal activities were introduced in late 1960s and 70s, remain the cornerstone of treatment of superficial and deep fungal infections. They exhibit high efficacy with low toxicity and also possess immediate action. Newer antifungal agents introduced lately are now being preferred mostly as topical over the conventional imidazoline derivatives as they have shorter duration of action, more consistent absorption rate and longer period of retention in the infected tissues.[7]

We found that out of 35 patients, males were 18 and females were 17. There was significant difference in size

of lesion in all days (P< 0.05). There was significant difference in size of lesion in all days (P< 0.05).

Luliconazole is one such recently introduced topical (1%) imidazoline derivative, approved in November 2013 by US Food and Drug Adminstration (FDA) for treatment of tinea cruris, interdigital tinea pedis and tinea corporis and has better efficacy, tolerability and shorter duration of treatment as it shows more effective inhibition of ergosterol and stays longer in stratum corneum. It inhibits ergosterol biosynthesis by inhibiting lanosterol 14 alpha demethylase. Since ergosterol is a essential component of cell membrane and its disruption alter fluidity and integrity of cell membrane and cell wall resulting in inhibition of fungal growth. Additionally luliconazole inhibit the production of proteases by trichophyton species.[8]

Luliconazole possess unique structure as imidazoline moiety is incorporated into ketene dithioacetate structure similar to lanconazole and its R enantiomer is only active while S enantiomer is inactive and possess more potent antifungal activity than lanconazole. It is primarily metabolized by CYP2D6 and CYP3A4 and is 90% bound to plasma proteins. Diseased skin facilitates its more absorption as compared to healthy intact skin, thus Luliconazole have high Cmax and AUC in tinea cruris. It has better safety profile, mild application site reactions are observed in less than 1% population including dermatitis and cellulitis.[9]

Amorolifine**,** a morpholine derivative is one such topical preparation. It inhibits D-14 reductase and D7–D8 isomerase, which deplete ergosterol biosynthesis and causes ignosterol to accumulate in fungal cell membrane. This alteration in membrane sterol content results in changes in permeability and disruption of essential metabolic processes required for fungal integrity. It possesses potent fungistatic and fungicidal action (Topical formulation of Amorolifine as (0.25%) cream has been recently introduced in Indian market for use in tinea corporis.[10]

CONCLUSION

Authors found that both 1% Luliconazole and 0.25% Amorolifine were effective in management of tinea corporis.

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