

Assessment of the Effectiveness of Topical Agents in Treating Tinea Corporis and Tinea Cruris

Prerna

Senior Resident, Department of Dermatology, Government Medical College and Hospital, Purnia, Bihar, India

Received: 02-01-2024 / Revised: 11-02-2024 / Accepted: 10-03-2024

Corresponding Author: Dr. Prerna

Conflict of interest: Nil

Abstract

Aim: To compare the effectiveness of topical amorolfine, luliconazole, tetraconazole, and terbinafine in treating tinea corporis and tinea cruris.

Materials and Methods: It was a retrospective, randomized, open-labeled, parallel group study was conducted Department of Dermatology, GMCH, Purnia, Bihar, India. It was a pragmatic study to assess the therapeutic response to certain topical antifungals in the current scenario of dermatophytosis. Clinically diagnosed healthy adult patients with tinea corporis and tinea cruris requiring topical antifungal therapy were selected for the study. Patients aged 18 years or above with localized tinea corporis or cruris without any form of prior treatment for at least a week were chosen. An arbitrary sample size of 80 was considered with 20 patients in each category of antifungal was considered. Consecutive eligible patients were prescribed topical amorolfine (0.25%), luliconazole (1%), tetraconazole (2%) and terbinafine (1%) in a serial order. Same brand of the topical drug was used throughout the period of study. Amorolfine and luliconazole were advised once daily while tetraconazole and terbinafine was twice daily application.

Results: Mean age of these patients was 34 years with youngest being 18 years and oldest 70 years. Male to female (35 versus 32) ratio was 1.1:1. We had 13 drop outs despite telephonically contacting the patients for follow up. Luliconazole showed best improvement of pruritus (mean-1.47), erythema (mean-1.53) and scaling (mean- 1.53). Terbinafine showed the least improvement with mean being 0.73, 0.60, 0.67 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 ($P = 0.020$) and highly significant for erythema and scaling ($P = 0.004$ & 0.007). Based on the improvement of all three parameters, we categorized the patients into three groups. 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 12 patients (66%) 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 ($P = 0.018$, Fisher's exact test).

Conclusion: We believe that Luliconazole may score over other 3 topical antifungals, however studies involving larger number is required to confirm these findings. Although it belongs to azole class, it seems to exhibits fungicidal activity.

Keywords: Topical Amorolfine, Luliconazole, Tetraconazole, And Terbinafine Treating Tinea Corporis, Tinea Cruris.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Tinea corporis (ringworm of the body) and tinea cruris (jock itch) are common fungal infections of the skin caused primarily by dermatophytes, including *Trichophyton* and *Epidermophyton* species. These infections present as circular, erythematous lesions with raised edges and central clearing, affecting various body areas, including the trunk, extremities, and groin. Topical antifungal agents play a crucial role in the treatment of these

dermatophyte infections, offering effective and targeted therapy while minimizing systemic side effects. Topical antifungals exert their therapeutic effect by disrupting fungal cell membrane integrity or inhibiting fungal enzyme activity, thereby interfering with fungal growth and replication. Amorolfine, luliconazole, tetraconazole, and terbinafine are among the widely used topical agents, each offering unique mechanisms and therapeutic profiles tailored to specific fungal

strains and clinical presentations. [1,2] Amorolfine is a broad-spectrum antifungal agent that inhibits ergosterol synthesis, an essential component of fungal cell membranes. It is effective against dermatophytes, yeasts, and moulds. Clinical studies have demonstrated its efficacy in treating tinea corporis and tinea cruris, with high cure rates and good tolerability. Amorolfine's broad antifungal spectrum makes it a valuable option for cases resistant to other topical treatments. Luliconazole is a newer azole antifungal that inhibits fungal lanosterol 14 α -demethylase, an enzyme crucial for ergosterol synthesis. It exhibits potent fungicidal activity against various dermatophyte species, including those causing tinea corporis and tinea cruris. Studies have shown luliconazole's efficacy in achieving rapid symptom relief and mycological cure, with low recurrence rates. Its favourable safety profile and convenient once-daily application enhance patient compliance and treatment outcomes. [3,4] Tetraconazole is a broad-spectrum imidazole antifungal that inhibits ergosterol synthesis and exerts anti-inflammatory effects. It demonstrates efficacy against dermatophytes, yeasts, and some gram-positive bacteria. Clinical trials have validated its effectiveness in treating tinea corporis and tinea cruris, emphasizing its dual action against fungal infection and associated inflammation. Sertaconazole's anti-inflammatory properties contribute to symptom relief, making it suitable for inflammatory forms of these dermatophyte infections. Terbinafine is an allylamine antifungal agent that disrupts fungal cell membrane function by inhibiting squalene epoxidase, an enzyme crucial for ergosterol biosynthesis. It exhibits fungicidal activity against dermatophytes and is effective in treating tinea corporis and tinea cruris, often requiring shorter treatment durations compared to other topical agents. Terbinafine's rapid onset of action and high cure rates make it a preferred choice for uncomplicated fungal infections of the skin. [5,6]

Materials and Methods

It was a retrospective, randomized, open-labeled, parallel group study was conducted Department of Dermatology, GMCH, Purnia, Bihar, India for one year. It was a pragmatic study to assess the therapeutic response to certain topical antifungals in the current scenario of dermatophytosis. Clinically diagnosed healthy adult patients with tinea corporis and tinea cruris requiring topical antifungal therapy were selected for the study. Patients aged 18 years or above with localized tinea corporis or cruris without any form of prior treatment for at least a week were chosen. 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 80 was considered with 20 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%), tetraconazole (2%) and terbinafine (1%) in a serial order. Same brand of the topical drug was used throughout the period of study. Amorolfine and luliconazole were advised once daily while tetraconazole 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. Clinical images of consented patients were taken at starting of therapy and at 3 weeks with due care that the patient's identity was not revealed. Antihistamine tablet levocetirizine 5 mg at bed time was given for 7 days to all patients as an anti-pruritic medication.

Results

Among the total 80 patients, 67 reported at the 3 week follow up. Among them 30 were treatment naive, 16 were topical steroid (with or without antifungal) modified cases, 14 were partially treated with antifungals and 7 had used home remedies prior to the study (Table 1). Mean age of these patients was 34 year with youngest being 18 years and oldest 70 years. Male to female (35 versus 32) ratio was 1.1:1. We had 13 drop outs despite telephonically contacting the patients for follow up. Luliconazole showed best improvement of pruritus (mean-1.47), erythema (mean-1.53) and scaling (mean- 1.53). Terbinafine showed the least improvement with mean being 0.73, 0.60, 0.67 for pruritus, erythema and scaling respectively.[Table 2] Difference in the mean values of improvement of luliconazole as compared to the other three drugs was significant for pruritus ($P = 0.020$) and highly significant for erythema and scaling ($P = 0.004$ & 0.007). Based on the improvement of all three parameters, we categorized the patients into three groups. [Table 3] 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 12 patients (66%) 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 (P = 0.018, Fisher's exact test).

Table 1: Previous topical treatment

Group	Naive	Steroid	Antifungal	Others
Amorolfine	5	8	3	2
Luliconazole	9	3	6	1
Sertaconazole	8	3	2	2
Terbinafine	8	2	3	2
Total	30	16	14	7

Table 2: Comparison between pruritus, erythema & scaling

Parameters	Group	N	Mean	P value	
Pruritus	Amorolfine	18	1.06	0.020	Sig
	Luliconazole	19	1.47		
	Sertaconazole	15	1.13		
	Terbinafine	15	0.73		
Erythema	Amorolfine	18	0.89	0.004	Hs
	Luliconazole	19	1.53		
	Sertaconazole	15	1.13		
	Terbinafine	15	0.60		
Scaling	Amorolfine	18	0.83	0.007	Hs
	Luliconazole	15	1.53		
	Sertaconazole	19	1.20		
	Terbinafine	18	0.67		
Total	Amorolfine	18	2.78	0.009	Hs
	Luliconazole	19	4.53		
	Tetraconazole	15	3.47		
	Terbinafine	15	2.00		

Table 3: Group comparison of drugs

Response	Amorolfine		Luliconazole		Sertaconazole		Terbinafine	
	N	%	N	%	N	%	N	%
Poor	7	38.9	2	10.5	3	20.0	7	46.7
Moderate	7	38.9	5	26.3	7	46.7	7	46.7
Good	4	22.2	12	63.2	5	33.3	1	6.7
Total	18	100.0	19	100.0	15	100.0	15	100.0

N= Number of patients
 Poor = Total scores 0,1,2, Moderate = Total scores 3,4, Good = Total scores 5,6

Discussion

Topical antifungal therapy is the mainstay in the treatment of dermatophytosis; however increased number of extensive infections in the recent times has been a limiting factor. Newer topical antifungals seem to have certain advantages over the older drugs. [6] Dermatologist treating dermatophytosis has less information about the efficacy of the currently available topical therapies. Current epidemic of dermatophytosis is complicated by an increased number of chronic and recurrent dermatophytosis. [7] Topical steroid abuse also seems to be a major contributor to the onslaught of extensive and treatment resistant cases. [8] There has also been a shift in the dominant pathogen responsible for the infections across India from *Trichophyton rubrum* to

Trichophyton mentagrophytes. [9] Thus current circumstances are different than a decade ago and we need more information about the response to the therapeutic agents. We conducted this study in 80 adult patients but only 67 completed the study. There was almost equal number of patients in both genders and the sample represented almost all age groups. Only 30 patients were treatment naive. Others used some form treatment that included topical steroids with or without antifungal (16 patients) or antifungal alone (14) which were bought over the counter (OTC) or prescribed by the local practicing doctors. We found less OTC drug usage in our patients compared to another study but still it was sizable. [10] We found that the topical antifungals were effective in majority of the patients, alt-

though variable response was seen. Best response at the end of 3 weeks of topical therapy was shown by luliconazole for all three parameters pruritus, erythema and scaling, and the results were statistically significant. Jerajani et al conducted almost a similar study and found tetraconazole exhibiting better response than luliconazole and terbinafine. Another study conducted by Choudhary et al showed equal efficacy between tetraconazole and terbinafine. [11] Improvement was assessed on the basis of total score and 3 groups were made. Out of which luliconazole had 12 patients with good response followed by tetraconazole (5), amorolfine (4) and terbinafine (1) least. This indicates that luliconazole could be the most effective topical antifungal as compared to the other three currently available drugs. This high efficacy may be due to its low MIC as compared to certain other antifungals for *T. rubrum* and *T. mentagrophytes*. There seem to be a poor response to the fungicidal drug terbinafine which could be due to various factors that may include drug resistance. [12-15] Strength of this study lies in replicating the current scenario of dermatophytosis in the study by including naïve as well as partially treated or mistreated cases. We compared currently available relatively new molecules whose efficacy is less known in the current Indian scenario. Limitation of the study lies in the recruitment of less number of cases. This is primarily due to lesser availability of suitable cases that require only topical treatment despite a large load of dermatophytosis in the daily dermatological practice. Result obtained in the study needed to be validated with inclusion of large number of cases with a better design that could include blinding of the dispensed drug.

Conclusion

We believe that Luliconazole may score over other 3 topical antifungals, however studies involving larger number is required to confirm these findings. 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. Topical antifungal therapies can also have a synergy or additives with systemic antifungals. Hence topical antifungals are the integral part of management of the glabrous tinea infections.

References

1. Agrawal V, Manjunath Shenoy M, Pinto M, Amina Asfiya M I, Hegde S, Comparative study of efficacy of topical amorolfine, luliconazole, tetraconazole, terbinafine in tinea

- corporis and tinea cruris. *IP Indian J Clin Exp Dermatol* 2019;5(2):111-115.
2. Paul C, Baran R, Mommeja-Marin H, et al. A double-blind, randomized controlled trial comparing the efficacy and safety of luliconazole with that of ketoconazole cream 2% in the treatment of tinea pedis. *J Am Acad Dermatol*. 2012;66(5 Suppl 1). doi:10.1016/j.jaad.2011.11.091.
3. Pillai R, Bueno JR, Peiris L, Fasanmade A, Calimlim B. Efficacy and safety of sertaconazole nitrate 2% cream compared with fluconazole 150 mg tablet in tinea corporis/tinea cruris: a pooled analysis. *Mycoses*. 2017;60(6):380-388. doi:10.1111/myc.12611.
4. Sahoo AK, Mahajan R. Management of tinea corporis, tinea cruris, and tinea pedis: a comprehensive review. *Indian Dermatol Online J*. 2016;7(2):77-86. doi:10.4103/2229-5178.178099.
5. Kumar, Laxman, et al. "A comparative study of topical amorolfine, sertaconazole and terbinafine in patients with tinea corporis and tinea cruris." *European Journal of Molecular and Clinical Medicine*, vol. 9, no. 1, Wntr 2022, pp. 74+.
6. Sahni K, Singh S, Dogra S. Newer topical treatments in skin and nail dermatophyte infections. *Indian Dermatol Online J* 2018; 9:149-58.
7. Dogra S, Uprety S. The menace of chronic and recurrent dermatophytosis in India: Is the problem deeper than we perceive? *Indian Dermatol Online J* 2016; 7:73-6.
8. Verma S, Madhu R. The great Indian epidemic of superficial dermatophytosis: An appraisal. *Indian J Dermatol* 2017; 62:227-36.
9. Mala MS. Mellow to the malicious: Could Trichophyton mentagrophytes be the malefactor? *Clin Dermatol Rev* 2017;1(S1):1-2.
10. Dabas R, Janney MS, Subramaniyan R, Arora S, Lal V S, Donaparthi N et al. Use of over-the-counter topical medications in dermatophytosis: A cross-sectional, single-center, pilot study from a tertiary care hospital. *Indian J Drugs Dermatol* 2018; 4:13-7.
11. Choudhary SV, Bisati S, Singh AL, Koley S. Efficacy and safety of terbinafine hydrochloride 1% cream vs. sertaconazole nitrate 2% cream in tinea corporis and tinea cruris: A comparative therapeutic trial. *Indian J Dermatol* 2013; 58:457-60.
12. Rudramurthy SM, Shankarnarayan SA, Dogra S, Shaw D, Mushtaq K, Paul RA, et al. Mutation in the Squalene Epoxidase Gene of Trichophyton interdigitale and Trichophyton rubrum Associated with Allylamine Resistance. *Antimicrob Agents Chemother* 2018; 26:62(5). pii: e02522-17.

13. Khanna D, Bharti S. Luliconazole for the treatment of fungal infections: an evidence-based review. *Core Evid* 2014; 9:113- 24.
14. Rotta I, Ziegelmann PK, Otuki MF, Riveros BS, Bernardo NL, Correr CJ et al. Efficacy of topical antifungals in the treatment of dermatophytosis: a mixed-treatment comparison meta-analysis involving 14 treatments. *JAMA Dermatol* 2013;149(3):341-9.
15. Gupta AK1, Kohli Y. In vitro susceptibility testing of ciclopirox, terbinafine, ketoconazole and itraconazole against dermatophytes and nondermatophytes, and in vitro evaluation of combination antifungal activity. *Br J Dermatol* 2003;149(2):296-05.