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A Novel Therapeutic Combination of Luliconazole 1% Cream and 30% Salicylic Acid Peel in Superficial Dermatophytosis Management

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Abstract:

Abstract: Background: Superficial dermatophytosis is a common fungal infection with high recurrence rates, necessitating effective treatment strategies. Objective: To compare the efficacy and safety of combination therapy with 30% salicylic acid peel in superficial dermatophytosis. Methods: This interventional, prospective, follow-up study enrolled 160 patients with superficial dermatophytosis received combination therapy with 30% salicylic acid peel and luliconazole 1% cream. Results: The combination therapy group showed significant improvement in PASI score reduction ($p<0.01$) and faster recovery. Pruritus reduction was observed in all patients receiving therapy. Conclusion: The combination of 30% salicylic acid peel with luliconazole 1% cream in dermatophytosis, offers improved efficacy and faster recovery with minimal side effects.

Introduction

The clinicians of India have witnessed a disconcerting surge in the incidence of chronic, recalcitrant, and recurrent cases of superficial dermatophytosis that often prove unresponsive to conventional pharmacotherapeutic regimens and dosages of recommended antifungal treatments.[1]This transformed clinical visage of dermatophytosis has engendered a state of veritable panic among the dermatological community, with the sheer chronicity of these conditions afflicting patients in a manner unprecedented for any other dermatological malady in the country. Indeed, the contemporary prevalence of dermatophytosis in India has been reported to range from 36.6% to a staggering 78.4%.[2]

Despite the availability of multiple consensus statements delineating the management of dermatophytosis, diverse therapeutic approaches have been trialed in the Indian context, necessitating closer scrutiny to further refine the guidelines and ameliorate patient care.[3]

In this context, luliconazole, a novel imidazole antifungal, holds promise. Luliconazole has demonstrated potent in vitro activity against dermatophytes and Candida, and has been clinically evaluated for the treatment of tinea pedis, cruris, and corporis.[4] Notably, while azole antifungals are generally considered fungistatic, luliconazole exhibits a fungicidal effect against Trichophyton species in the context of dermatophytosis.[5]

Fungal infections like tinea corporis pose significant treatment challenges. One major obstacle is the ability of fungi to adapt to antifungal drugs, rendering them ineffective over time. Furthermore, the spores of dermatophytes can reside deep within hair follicles, making conventional treatments unsuccessful in fully eradicating the infection. Additional risk factors, including infection by non-anthropophilic dermatophytes, prior corticosteroid exposure, and excoriation, can also lead to treatment resistance. Moreover, the infection can spread to the hair shafts and keratinized portions, such as Adamson's fringe, contributing to the chronic nature of these infections. [6]

In light of these challenges, the need for newer, more cost-effective, and better-tolerated treatment modalities has become increasingly evident. One such approach involves the use of topical keratolytic agents, such as salicylic acid, which may act synergistically with topical antifungals to enhance their efficacy in the management of hyperkeratotic dermatophytosis.[7] Moreover, as the keratinophilic dermatophytes primarily reside within the stratum corneum, the peeling of this superficial layer may facilitate the removal of the causative fungal elements.[6]

Cognizant of these considerations, the present study was undertaken to ascertain whether the combination of luliconazole 1% cream and 30% salicylic acid peel would prove superior to the use of luliconazole 1% cream alone in the treatment of superficial dermatophytosis.

Materials and Method

This study is an interventional, prospective, follow-up study that aims to investigate the effectiveness of combination treatment for superficial dermatophytosis. The study population consists of patients visiting the dermatology outpatient department at PCMS & RC, diagnosed with superficial dermatophytosis. A total of 160 patients were recruited for the study, which was conducted from November 2022 to December 2023.
The study obtained ethical permission from the institutional ethical committee and informed written consent from all enrolled patients. The inclusion criteria for the study were: patients who gave their consent, were over 18 years old, had a positive 10% KOH mount for fungus, and had less than 20% body surface area involvement. The exclusion criteria were: pregnant females, patients under 18 years old, negative KOH mount for fungus, patients with more than 20% body surface area involvement, those who used oral antifungals within the preceding two weeks, and patients allergic to luliconazole cream.

Subjects were counseled about the disease and informed consent was obtained. Patients were explained about the voluntary nature of the research and that they have an option to out of the research during the research period. Those patients who were willing to participate and can come for treatment once a week for a period of one month was given combination therapy of luliconazole 1% cream and 30% salicylic acid peel.

A detailed history and clinical examination were done and PASI score was calculated at Day 1 and at end of study. Lesions was photographed at the start and end of the study. Patients were evaluated by 10% KOH MOUNT by taping method –by applying cellophane tape over the skin lesion pressing firmly, removing it and sticking to sterile glass slide over which 3-4 drops of 10% KOH solution was placed and observed under microscope.

Before procedure the respective lesions with 1 cm beyond their diameter were cleaned by normal saline. Petroleum jelly was applied near all mucosal openings.

Salicylic acid 30% was prepared by adding 500 mL propylene glycol solution to 150 g of salicylic acid powder. Salicylic acid 30% application was done over the lesions (and 1 cm beyond the lesional border). The maximum quantity of salicylic acid use during a single treatment session was 10 mL (3 g of salicylic acid). Salicylic acid crystallizes forming a pseudo-frost which was washed with water after three to five minutes. In case of any skin irritation, ice pack application was done.

Patient were counselled to apply 1% luliconazole twice daily upto 1cm beyond lesion for 1 month. The treatment was repeated every week (with a delay of up to 3 days considered acceptable) for 4 weeks. Thereafter, the patients were followed up after one month.

Mean and standard deviation for quantitative data was applied. Frequency and percentage for qualitative data was applied after data was collected. Data obtained was analyzed using Chi-square test, Fishers exact test and Friedman test, whereas pair-wise comparison was done by Wilcoxon signed rank test and Mann-Whitney test.

Results

Table 1: *Age group wise distribution of study subjects in the groups*

Variables		30% salicylic acid with luliconazole 1% cream (n=160)		Chi square value
		Frequency	Percent	
Age	<20	11	6.9	4.75; p value – 0.44
	21-30	25	15.6	
	31-40	47	29.4	
	41-50	44	27.5	
	51-60	22	13.8	
	>60	11	6.9	
Gender	Female	72	45.0	-2.92; p value – 0.87
	Male	88	55.0	
-	Total	160	100.0	-

The mean age distribution in this study indicates that dermatophytosis is most common in the third decade of life. The majority (60%) of patients were in the 21–40 year age group. The gender wise distribution of study subjects in the groups results revealed that total 57 female in group 1 and 72 female in gorup 2 and 103 female in group 1 and 88 male in group 2 participated in the study it was found statistically non significant (p=0.87) (table 1).

Table 2: *Comparison of mean difference PASI score at end of study of study subjects in the groups*

Group	Mean	Std. Deviation
30% salicylic acid with luliconazole 1% cream	2.81	1.63

Table 2 shows comparison of mean difference PASI score at end of study of study subjects in the groups results revealed that mean difference PASI score was found 1.55 in group 1 and 2.81 in group 2 it was found statistically significant (P<0.01).

Table 3: *Mean difference PASI score range at end of study of study subjects in the groups*

Decrease in mean difference PASI score range	Group 2 (n=160) 30% salicylic acid with luliconazole 1% cream	
	Frequency	Percent
0-0.5	0	0.0
0.6-1	16	14.2
1.1-1.5	24	21.2
1.6-2	14	12.4
2.1-2.5	22	19.5
2.6-3	37	32.7
Total#	113	100.0

Table 3 shows comparison of mean difference PASI score range at end of study of study subjects in the groups results revealed that of mean difference PASI score range 0-0.5 found in 47 subjects of group 1 , 0.6-1 found in57 subjects of group 1 and 16 subjects of group 2, 1.1-1.5 in 8 subjects of group 1 and 24 subjects of group 2, 1.6-2 in 3 subjects of group 1 and 14 subjects of group 2, 2.1-2.5 in 5 subjects of gorup 1 and 22 subjects of gorup 2 and 2.6-3 in 3 subjects of group 1 and 37 subjects of group 2 it was found statistically significant (p<0.01). Subjects whose PASI score was not recorded at the end of study due to dropout were excluded.

Table 4: *Side effects wise distribution of study subjects in the groups*

Side effects	30% salicylic acid with luliconazole 1% cream	
	Frequency	Percent
None	116	72.5
Burning during application of peel	39	24.37
Development new lesion on the unaffected side of the buttock	1	0.62
Irritant dermatitis	2	1.25
Maceration	1	0.62
Mild burning during application of peel with hyperpigmentation over the affected area.	1	0.62

Table 4 shows side effects wise distribution of study subjects in the groups results revealed that burning during application of peel was found in 39 subjects of group 2, development new lesion on the unaffected side of the buttock was found in one subject of group 2, irritant dermatitis was found in 2 subjects of group 2, maceration was found in one subject of group 2 and Mild burning during application of peel with hyperpigmentation over the affected area was found in one subject of group 2 remails all study participant did not showed any side affect it was found statistically non significant (P=0.07).

Discussion

The findings of this study demonstrate the efficacy of combination therapy using 30% salicylic acid peel with luliconazole 1% cream in the treatment of superficial dermatophytosis. This combination approach addresses multiple aspects of fungal infection management simultaneously, providing a comprehensive treatment strategy for patients with dermatophyte infections.

Efficacy of Combination Therapy
The significant reduction in PASI scores observed in patients treated with the combination therapy (from 3.63±1.72 to 0.82±0.82) demonstrates the therapeutic potential of this approach. The mean difference in PASI score of 2.81±1.63 indicates substantial clinical improvement in patients receiving this treatment regimen.

Our findings align with those of Kharkar RD et al, who examined a fixed-dose combination cream containing luliconazole 1% and salicylic acid 3% over a 2-week period, reporting a significant decrease in overall symptom score from 7.19±1.91 to 3.15±1.12 ($p<0.05$) with a 78% clinical improvement rate. Similarly, Brinda K et al reported significant reduction in lesion size and hyperpigmentation with 30% salicylic acid, supporting its use as an adjuvant in dermatophytosis treatment.

Mechanism of Action
The efficacy of the combination therapy can be attributed to the complementary mechanisms of action of both components. While luliconazole provides potent antifungal activity, salicylic acid contributes multiple beneficial effects:

1. Keratolytic Properties: Salicylic acid dissolves the intercellular cement that connects skin cells, facilitating the penetration of antifungal agents into deeper layers of the skin where the dermatophytes reside.
2. pH Modulation: By lowering the pH of the stratum corneum, salicylic acid increases moisture and promotes skin softening, creating an environment less favorable for fungal growth.
3. Anti-inflammatory Effects: As noted by Brinda K et al, salicylic acid helps reduce itching sensations, providing symptomatic relief to patients.
4. Antimicrobial Activity: At certain concentrations, topical salicylates demonstrate bacteriostatic and bactericidal effects against yeast and bacteria, potentially addressing secondary infections.

Gujjar SM et al specifically highlighted that the keratolytic and anti-inflammatory properties of 30% salicylic acid may potentiate antifungal action in tinea infections, which is consistent with our observations.

Clinical Improvements

A notable finding was the significant reduction in pruritus and hyperkeratosis of plaques after the first salicylic acid application in most patients. This rapid improvement in symptoms contributes to better patient comfort and potentially enhances treatment adherence.
The enhanced penetration of luliconazole facilitated by salicylic acid's keratolytic effect likely accounts for the favorable clinical outcomes in patients receiving this combination therapy. By effectively removing the hyperkeratotic barrier, salicylic acid allows luliconazole to reach its target site more efficiently, resulting in more effective fungal eradication.

Safety Profile

The combination therapy was generally well-tolerated, with no side effects reported in 72.5% of patients. The side effects that did occur were predominantly mild, including mild burning sensation during peel application (23.12%), with only 1.25% reporting severe burning. Other minor side effects included irritant dermatitis (1.25%), new lesions on unaffected areas (0.62%), maceration (0.62%), and hyperpigmentation (0.62%).

It is noteworthy that patients who cleaned the treatment area with normal saline before salicylic acid application reported fewer burning sensations, suggesting that proper pre-treatment skin preparation can minimize adverse effects. The safety profile observed in our study is consistent with findings by Bari AU et al, who reported that chemical peeling with salicylic acid was well-tolerated in various superficial dermatoses.

Clinical Implications

The efficacy of this combination therapy approach has significant implications for clinical practice, particularly in the context of increasing resistance to antifungal drugs. By enhancing the efficacy of luliconazole through the addition of salicylic acid, this combination therapy may help address the challenges posed by difficult-to-treat dermatophyte infections.

The rapid improvement in symptoms offered by the combination therapy may improve patient compliance and satisfaction, which are crucial factors in successful dermatophytosis management. Additionally, the cost-effectiveness of salicylic acid, as noted by Saoji V et al, makes this combination approach an economically viable option for many patients.

Limitations and Future Directions

A limitation of our study was non-compliance in some patients in the combination therapy group, with delays of more than 10 days for peel application resulting in drop-out cases. Future studies could explore strategies to improve patient adherence to the treatment regimen.

Additionally, while our study demonstrated efficacy of the combination therapy, further research is needed to evaluate long-term outcomes and recurrence rates. Saoji V et al reported a 41% recurrence rate after 4 weeks with salicylic acid peel treatment, highlighting the need for extended follow-up periods in future studies.

Conclusion

The combination of 30% salicylic acid peel with luliconazole 1% cream represents a promising approach for the management of superficial dermatophytosis. The complementary mechanisms of action of these agents, along with their favorable safety profile, make this combination a valuable addition to the therapeutic armamentarium against dermatophyte infections. The significant reduction in PASI scores and rapid improvement in clinical symptoms suggest that this combination therapy effectively addresses both the fungal infection and the associated hyperkeratotic changes in the skin.

Further studies with larger sample sizes and longer follow-up periods are warranted to confirm these findings and explore the potential of this combination therapy in recalcitrant or resistant cases of dermatophytosis. Considering the rising challenges of antifungal resistance and the limitations of current treatment options, this combination approach offers a promising alternative that merits further investigation in clinical practice.

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