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Original Research Article

Comparative Study of 1% Terbinafine Hydrochloride Ointment Vs 1% Naftifine Hydrochloride Ointment in Patients with Tinea Cruris

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Abstract

Aim: The aim of the present study was to compare the efficacy and safety of 1% Terbinafine HCl ointment with 1% Naftifine HCl in patients with Tinea cruris.

Methods: This study was done in the Department of Pharmacology and Department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna for one year. The study was conducted after approval from Institutional Ethical Committee, Patna Medical College, Patna.

Results: The difference between these two groups in terms of demographic details was not statistically significant. Most of the study participants had presented with multiple lesions in both group A (terbinafine group) and group B (butenafine group). The difference between these two groups was not statistically significant. In group A (terbinafine group), erythema was present in 40 (100.0%) cases, scaling was present in 40 (100.0%) cases, central clearing was present in 34 (85%) cases, papule was present in 37 (92.5%) cases. The difference was not statistically significant ($p>0.05$) between two groups. The difference between the Clinical assessment score of the two groups was significant ($p=0.001$) after 1st and 2nd week. Transient burning sensation at the application site was found in one of 2 (5%) cases of Group A (terbinafine group); but it resolved spontaneously and did not require discontinuation of therapy. In contrast, no side effects were reported by Group B (butenafine group) participants. The difference was not statistically significant ($p>0.05$).

Conclusion: The present study concluded that there was significant difference between the mean clinical assessment score of the two groups at the end of 2 weeks treatment period. Butenafine produced the quickest result and clinical efficacy was much higher with butenafine cream than that of terbinafine cream and this difference was statistically significant. Therefore, treatment with butenafine 1% cream was reported superior to treatment with terbinafine 1% cream in case of tinea cruris.

Keywords: 1% Terbinafine HCl ointment, 1% Naftifine HCl, Tinea cruris

Introduction

Tinea cruris is a dermatophyte infection of the groin and is more common in men than in women probably because males perspire more than females, greater areas of occlusive skin where the scrotum is in contact with the thigh and clothing difference. [1] Transmission of Tinea cruris may occur via physical contact with arthroconidia which are generated from dermatophyte filaments. Arthroconidia can survive for years embedded in scales of hair and skin, recurrent outbreaks of infection may occur particularly in individuals with a compromised immune system. [2]

In the initiation and propagation of Tinea cruris, environmental factors like warm and humid climate are also important and these cause increased outbreak of Tinea cruris infection in monsoon months in India.[1] In India, Tinea cruris infection is caused mainly by Trichophyton rubrum whereas in Western countries, Epidermophyton floccosum is the commonest dermatophyte. Till the 1940s, standard topical antifungal therapy was limited to Whitfield's ointment, Castellani's paint and Gentian violet. But today there are various modern topical antimycotics capable of eradicating human

dermatomycoses. Several classes of antifungal agents available are imidazole, triazoles and allylamines.[2] Other topical antimycotics includes Ciclopirox olamine, Selenium sulphide and Tolnaftate. [2]

Terbinafine is an allylamine which has a broad spectrum of antifungal activity. It interferes specially with fungal sterol biosynthesis at an early stage. [3] Butenafine is the only benzylamine class of antifungal agent with a structure and mode of action similar to allylamines. [4] Like the allylamines, Butenafine inhibits squalene epoxidation, blocking the biosynthesis of ergosterol, an essential lipid component of fungal cell membrane. The antifungal activity of both allylamine and benzylamine results from ergosterol deficiency and intracellular accumulation of squalene, which interferes with cell membrane function and synthesis. [3,4] Clinical cure of an uncomplicated tinea cruris infection usually can be achieved using topical antifungal agents. [5] Many topical antifungals of different groups are available for the treatment of dermatophytosis such as azole derivatives, allylamines, benzylamines, morpholine, etc. [6] The allylamines, including terbinafine and naftifine, contain a nitrogen atom and a neighboring double bond.

Terbinafine hydrochloride has broad spectrum of antifungal activity. It interferes with fungal sterol biosynthesis at an early stage. [7] Naftifine selectively inhibits the fungal enzyme squalene epoxidase, which is involved in the ergosterol biosynthesis pathway. [8] Ergosterol is a component of fungal cell membranes. Squalene epoxidase is also necessary for mammalian cholesterol biosynthesis, but naftifine is highly selective for fungal enzymes. Naftifine has minimal effects on mammalian cholesterol biosynthesis. [9] Naftifine has anti-inflammatory properties similar to azole medications plus 1 % hydrocortisone. [10] It has sustained fungicidal activity following treatment cessation because the levels of naftifine remain relatively unchanged in the epidermis several weeks post-treatment. Clinical response is highest 6 to 8 weeks post-treatment with naftifine. [11]

The aim of the present study was to compare the efficacy and safety of 1% Terbinafine HCl ointment with 1% Naftifine HCl in patients with Tinea cruris.

Materials and Methods

This study was done in the Department of Pharmacology and Department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna for one year. The study was conducted after approval from Institutional Ethical Committee, Patna Medical College, Patna.

Inclusion Criteria:

1. Patients of either sex

2. Age more than 14 years

3. Untreated patients of tinea cruris whose diagnosis was confirmed by potassium hydroxide (KOH) examination for fungal elements, and

4. Patients having at least three signs and symptoms of tinea cruris namely pruritus (symptom); polycyclic lesions, erythema, scaling, macerations, papules and vesiculation (signs).

Exclusion Criteria:

1. Patients who have received topical or oral antifungals either one to four weeks prior to the initiation of the study respectively,

2. Patients with history of hypersensitivity to allylamine or benzylamine anti-fungal agents,

3. Patients with any known severe systemic disease,

4. Immunocompromised status,

5. Pregnant or lactating women.

Study Design: This was a prospective open label study conducted in the department of Pharmacology, Patna Medical College, Patna in 80 patients of Tinea cruris visiting OPD of department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna over a period of 6 months fulfilling the inclusion criteria. Written informed consent was taken from all the patients included in my study.

Study Procedure: All potential patients were screened following the inclusion and exclusion criteria, then the first 80 patients who met these criteria and provide consent was enrolled in the study. Structured questionnaire was administered to gather valuable information about socio-demographic characteristics and disease-related information.

The patients was then randomized into two groups as group A (n=40) and group B (n=40) in a 1:1 ratio following a simple randomization method by allocating a code for each patient.

At the initial visit, all the study patients underwent detailed physical and cutaneous examination. All clinical details were recorded on a predesigned proforma. The symptoms and signs like erythema, scaling and pruritus were designated on a scale of 0 to 3 as follows: 0=none, 1=mild, 2=moderate and 3=severe. The individual symptom scores were added and a total score (clinical assessment score) was recorded.

Group A patients were treated with Terbinafine 1% cream and group B patients were treated with Naftifine 1% cream. Patients were advised to apply

the medication after bath to the affected sites and also to the surrounding areas, once daily for 2 weeks.

The patients were then clinically evaluated at the end of one and two weeks (i.e., at the end of treatment period). At each visit, thorough clinical examination was carried out and clinical assessment score was calculated to determine clinical efficacy. Adverse effects, if any, was also recorded at each visit. Clinical efficacy was defined in this study as reduction in the severity of symptoms and signs of tinea cruris (pruritus, erythema, scaling, etc.) as evident by decreased clinical assessment score from baseline during follow-up visit.

All data was collected at first using a structured paper-based questionnaire containing all the variables of interest. Data was then initially extracted in Microsoft Excel, coded, cleaned and then was entered into Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA) for further statistical analyses. The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test with Yates correction was used to analyze the categorical variables, shown with cross tabulation. Student t-test/unpaired t-test was used for continuous variables. P values <0.05 was considered as statistically significant.

Results

Table 1: Characteristics of the study participants

Characteristics	Group A (n=40) Number (%)	Group B (n=40) Number (%)	p values
Age in years			
<21	5 (12.5)	10 (25)	0.620
21−30	21 (52.5)	11 (27.5)	
>30	14 (35)	19 (47.5)	
Mean ± SD	31.88 ±11.08	30.40 ±9.51	
Sex			
Male	30 (75)	24 (85)	0.479^{ns}
Female	10 (25)	6 (15)	
Marital Status			
Married	22 (55)	26 (65)	0.563^{ns}
Single	18 (45)	14 (35)	
Educational Level			
Illiterate	2 (5)	2 (5)	0.628 ^{ns}
Primary School	5 (12.5)	10 (25)	
SSC	10 (25)	6 (15)	
HSC	10 (25)	5 (12.5)	
Graduate & above	13 (32.5)	17 (42.5)	
Occupation			
Service	24 (60)	13 (32.5)	0.345^{ns}
House wife	3 (7.5)	5 (12.5)	
Student	8 (20)	14 (35)	
Business	3 (7.5)	3 (7.5)	
Laborers	2 (5)	5 (12.5)	

Proportion of male was higher than female in group A (terbinafine group), which was 75% and 25% cases respectively. Same is also true for group B (butenafine group), where proportion of male versus female was 85% vs 15% cases respectively. The difference between these two groups was not statistically significant. Distribution of study participants on the basis of marital status showed that in group B (butenafine group), married persons were more than unmarried persons which was 26 (65%) cases and 14 (35%) cases respectively. Similar distribution was observed in group A (terbinafine group), where proportion of married and unmarried persons was 55% cases and 45% cases respectively. The difference between these two groups was not statistically significant. Majority of the patients of group A (terbinafine group) were graduate and above level followed by SSC, HSC, primary school and illiterate and similar pattern was observed among the patients of group B (butenafine group) where majority were graduate and above level followed by primary school, SSC, HSC, and illiterate. The difference between these two groups was not statistically significant. Service was the main occupation of the patients of group A (terbinafine group). In contrast, among the patients

of group B (butenafine group) majority were students followed by service, housewife, laborers and business. The difference between these two groups was not statistically significant.

Table 2: Presentation of Tinea cruris among the study participants

Characteristics	Group A (n=40) Number (%)	Group B (n=40) Number (%)	p values
Number of lesions			
Multiple	34 (85)	35 (87.5)	1.000
Single	6 (15)	5 (12.5)	
Clinical findings			
Erythema	40 (100)	38 (95)	0.312
Scaling	40 (100)	37 (92.5)	0.148
Central Clearing	34 (85)	30 (75)	0.269
Papule	37 (92.5)	34 (85)	0.333
Vesicles	14 (35)	16 (40)	0.770
Maceration	8 (20.0)	10 (25)	0.732
Pruritus	40 (100)	38 (95)	0.500

Most of the study participants had presented with multiple lesions in both group A (terbinafine group) and group B (butenafine group). The difference between these two groups was not statistically significant. In group A (terbinafine group), erythema was present in 40 (100.0%) cases, scaling was present in 40 (100.0%) cases, central clearing was present in 34 (85%) cases, papule was present in 37 (92.5%) cases. The difference was not statistically significant ($p>0.05$) between two groups.

Table 3: Comparative Clinical assessment score between the groups before and after treatment

Follow up & observation	Group A (Mean ± SD)	Group B (Mean ± SD)	P value
Base line	8.92±0.6	8.84±0.8	0.690
After 1st week	5.72±0.7	4.12±0.7	0.001
After 2nd week	3.04±0.5	1.44±0.9	0.001

The mean and standard deviation (SD) of clinical assessment score in group A (terbinafine group) and group B (butenafine group) were 8.92 ± 0.6 and 8.84±0.8 respectively before initiation of treatment. The difference between the mean score of two group was not significant ($p=0.690$). After one week of treatment the mean clinical assessment score with SD of group A (terbinafine group) and group B (butenafine group) participants were 5.72±0.7 and 4.12±0.7 respectively. The difference between the mean score of the two groups was significant ($p=0.001$). The mean clinical assessment score with SD in group A (terbinafine group) and group B (butenafine group) were 3.04±0.5 and 1.44±0.9 respectively after 2 weeks of treatment. The difference between the Clinical assessment score of the two groups was significant ($p=0.001$).

Table 4: Comparison of adverse effects among the treatment groups

Side effect	Group A (n=40) Number (%)	Group B (n=40) Number (%)	P value
Burning			
Yes	2 (5)	0 (0.0)	0.500
No	38 (95)	40 (100.0)	

Transient burning sensation at the application site was found in one of 2 (5%) cases of Group A (terbinafine group); but it resolved spontaneously and did not require discontinuation of therapy. In contrast, no side effects were reported by Group B (butenafine group) participants. The difference was not statistically significant ($p>0.05$).

Discussion

Tinea cruris, also known as jock itch, is an infection involving the genital, pubic, perineal, and perianal skin caused by pathogenic fungi known as dermatophytes. [12] These dermatophytes affect keratinized structures such as hair and the epidermis' stratum corneum resulting in a characteristic rash. Intertriginous areas are hospitable environments for fungus, with sweating, maceration, and alkaline pH being responsible for the groin's predilection for infection. [13] While tinea infections are often classified by the location of the body affected, they are also organized according to the responsible organism's primary source and mode of transmission. Geophilic, zoophilic, and anthropophilic fungi are found in and transmitted by soil, animals, and humans, respectively. [14] Autoinfection of dermatophytes is

also possible and especially crucial in tinea cruris as foot-to-groin spread can occur. [15] Tinea cruris is caused by dermatophytes belonging to three genera, Trichophyton, Epidermophyton, and Microsporum. [16] Cutaneous mycoses, including tinea cruris, affect 20 to 25 percent of the world's population. [17] Developing and tropical countries have an increased prevalence of dermatophyte infections secondary to high temperatures and increased humidity.

Proportion of male was higher than female in group A (terbinafine group), which was 75% and 25% cases respectively. Same is also true for group B (butenafine group), where proportion of male versus female was 85% vs 15% cases respectively. The difference between these two groups was not statistically significant. Distribution of study participants on the basis of marital status showed that in group B (butenafine group), married persons were more than unmarried persons which was 26 (65%) cases and 14 (35%) cases respectively. On the other hand, Jerajani et al [18] and Rotta et al [19] observed higher mean age in their respective studies, which were 36.49±14.70 years and 38.4±13.4 years respectively. The higher mean age might be due to geographical variations, racial, ethnic differences, genetic causes, different lifestyle and increased life expectancy. Most of the study participants had presented with multiple lesions in both group A (terbinafine group) and group B (butenafine group). The difference between these two groups was not statistically significant. In group A (terbinafine group), erythema was present in 40 (100.0%) cases, scaling was present in 40 (100.0%) cases, central clearing was present in 34 (85%) cases, papule was present in 37 (92.5%) cases. The difference was not statistically significant ($p>0.05$) between two groups.

Ramam et al [20] observed in the butenafine group, the clinical score declined from a mean of 7.36 at baseline to 1.5±1.43 at week 2, 1.04±1.55 at week 4, 1.45±2.3 at week 6 and 1.5±2.3 at week 8. The reduction in the sign and symptom score from baseline at 4 weeks post-treatment follow-up in the butenafine treated group was 81.5%.9 Similar findings were also reported by Singal et al [21] where they showed that mean clinical assessment score declined from 6.65±1.29 at baseline to 1.00±0.62 at 2nd week, 0.56±0.51 at 4th week and 0.65±0.49 at the end of 8th week in the group treated with butenafine. The mean and standard deviation (SD) of clinical assessment score in group A (terbinafine group) and group B (butenafine group) were 8.92 ± 0.6 and 8.84±0.8 respectively before initiation of treatment. The difference between the mean score of two group was not significant ($p=0.690$). After one week of treatment the mean clinical assessment score with SD of group A (terbinafine group) and group B (butenafine group) participants were 5.72±0.7 and 4.12±0.7 respectively. The difference between the mean score of the two groups was significant ($p=0.001$). The mean clinical assessment score with SD in group A (terbinafine group) and group B (butenafine group) were 3.04±0.5 and 1.44±0.9 respectively after 2 weeks of treatment. The difference between the Clinical assessment score of the two groups was significant ($p=0.001$). Transient burning sensation at the application site was found in one of 2 (5%) cases of Group A (terbinafine group); but it resolved spontaneously and did not require discontinuation of therapy.

In contrast, no side effects were reported by Group B (butenafine group) participants. The difference was not statistically significant ($p>0.05$). Similar findings were also reported by a study of Jerajani et al[18], where only one patient using terbinafine 1% cream had complained of burning sensation on application. This could be attributed to the pharmacological property of any topical antifungal drug or hypersensitivity to the study drug, that could not be assessed as the patient was lost to follow-up. [22]

Conclusion

The present study concluded that there was significant difference between the mean clinical assessment score of the two groups at the end of 2 weeks treatment period. Butenafine produced the quickest result and clinical efficacy was much higher with butenafine cream than that of terbinafine cream and this difference was statistically significant. Therefore, treatment with butenafine 1% cream was reported superior to treatment with terbinafine 1% cream in case of tinea cruris.

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