Original Article

Comparative Study of Topical Terbinafine 1% Cream versus Butenafine 1% Cream in the Treatment of Tinea Cruris

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Abstract

Background*: Tinea cruris constitutes a major health problem worldwide. Although not life-threatening, it can cause significant discomfort in daily activities. So, search for better therapeutic options in terms of clinical efficacy and safety profile is ongoing.* ***Objective****: To compare the efficacy and safety of topical terbinafine 1% and butenafine 1% cream in the treatment of tinea cruris.* ***Materials and Methods****: This Comparative interventional study was carried out in the Dermatology & Venereology department of Bangabandhu Sheikh Mujib Medical University between October 2014 and March 2015. A total of 50 patients of tinea cruris who met the inclusion criteria and provided consent were enrolled in the study. They were then divided into two groups as Group A (terbinafine group) and Group B (butenafine group) in a 1:1 ratio following a simple randomization method. Patients were advised to apply the medication once daily for 2 weeks and evaluated on the basis of clinical assessment score at the end of 1 and 2 weeks.* ***Results:*** *The baseline socio-demographic characteristics of the two groups were not statistically significantly different. Higher clinical cure was observed in butenafine recipients as compared with terbinafine recipients on the basis of mean clinical assessment score at the end of 7 days (5.72±0.7 vs 4.12±0.7) and 14 days (3.04±0.5 vs 1.44±0.9). The difference was statistically significant at both the time points. Both the drugs were well-tolerated except one patient of terbinafine group complained of transient burning.* ***Conclusion****: Treatment with butenafine 1% cream can be considered superior to terbinafine 1% cream in case of tinea cruris.*

Key words: *Tinea cruris; Dermatophytosis; Terbinafine cream; Butenafine cream*

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Introduction

Tinea cruris, a pruritic superficial fungal infection of the groin and adjacent skin, is the second most common clinical presentation for dermatophytosis. It is an important clinical problem that may, at times, be a diagnosticas well as therapeutic challenge.[1] Tinea cruris has a worldwide distribution but is found more commonly in hot, humid climates and affects individual of all age and sex.[2,3] It is a contagious infection transmitted by fomites or by autoinoculation from a reservoir on the hands or feet (tinea manuum, tinea pedis and tinea unguium). The most common etiologic agents for tinea cruris include Trichophyton rubrum and Epidermophyton floccosum; less commonly Trichophyton mentagrophytes and Trichophyton verrucosum are involved.[1]

Topical preparations with good local bioavailability

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are the commonly used and preferred first line agents in the treatment of localized dermatophytosis. Their improved efficacy aims to shorten the treatment period with fewer side effects. Ease of application, enhanced patient compliance, and minimal recurrences also add to the therapeutic response.[4] Quest for more potent and more compliant medication is going on. Finding a medication with more potency and capability to treat this disorder at less inconvenience will empower the dermatologist and the general physicians to fight the disorder with better efficacy.

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] Terbinafine hydrochloride is one of the fungicidal allylamine group of drugs with broad spectrum of antifungal activity. It interferes with fungal sterol biosynthesis at an early stage.[7] Butenafine hydrochloride is a novel, benzylamine derivative with a chemical structure and mode of action is similar to allylamine antifungals.[8] It likes the allylamines, butenafine also 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 fungal cell membrane function and synthesis.[7,8]

The dermatophytes responsible for tinea cruris have been shown to be susceptible to both terbinafine and butenafine.[9,10] However, comparative study between topical terbinafine 1% and butenafine 1% cream in the treatment of tinea cruris is lacking. Under these circumstances, the current study was undertaken to compare the efficacy and safety of topical terbinafine 1% and butenafine 1% cream in the treatment of tinea cruris.

Materials and Methods

This prospective, randomized, open-labeled comparative interventional study was conducted on 50 patients over the age of 14 years who visited Dermatology and Venereology outpatient department of Bangabandhu Sheikh Mujib Medical University (BSMMU) duringthe period of October 2014 to March 2015, a duration of 6 months. The inclusion criteria comprised of untreated patients of tinea cruris whose diagnosis was confirmed by potassium hydroxide (KOH) examination for fungal elements and who had at least three signs and symptoms of tinea cruris namely pruritus (symptom); polycyclic lesions, erythema, scaling, macerations, papules and vesiculation (signs). Patients were excluded from the study, if they had received topical or oral antifungals either one to four weeks prior to the initiation of the study respectively, history of hypersensitivity to allylamine or benzylamine anti-fungal agents, any known severe systemic disease, immunocompromised status, pregnant or lactating women.

All potential patients were screened following the inclusion and exclusion criteria, then the first 50 patients who met those criteria and provided consent were enrolled in the study. Informed written consent was at first obtained from all the patients, then a structured questionnaire was administered to gather valuable information about socio-demographic characteristics and disease-related informations.

The patients were then randomized into two groups as group A (n=25) and group B (n=25) in a 1:1 ratio following a simple randomization method by allocatinga 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

butenafine 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, were 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 were collected at first using a structured paper-based questionnaire containing all the variables of interest. Data were then initially extracted in Microsoft Excel, coded, cleaned and then 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 were considered as statistically significant.

Results

There was a total of 50 patients, 25 patients in the terbinafine group (Group A) and 25 patients in the butenafine group (Group B). In group A (terbinafine group), majority of the patients were in the age group of 21−30 years. In group B (butenafine group), majority of the patients were in the age group of >30 years. The mean age with SD in group A (terbinafine group) and group B (butenafine group) were 31.88±11.08 years and 30.40±9.51 years respectively. The difference between the age of two group was not statistically significant (p=0.614).

Proportion of male was higher than female in group A (terbinafine group), which was 76.0% and 24.0% cases respectively. Same is also true for group B (butenafine group), where proportion of male versus female was 84.0% vs16.0% cases respectively. The difference between these two groups was not statistically significant (p=0.479).

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 16 (64.0%) cases and 9 (36.0%) cases respectively. Similar distribution was observed in group A (terbinafine group), where proportion of married and unmarried persons was 56.0% cases and 44.0% cases respectively. The difference between these two groups was not statistically significant (p=0.563).

Majority of the patients of group A (terbinafine group) were graduate and above level which was 9 (36.0%) cases followed by SSC, HSC, primary school and illiterate which were 6 (24.0%) cases, 6 (24.0%) cases, 3 (12.0%) cases and 1 (4.0%) case respectively. Somewhat similar pattern was observed among the patients of group B (butenafine group) where majority were graduate and above level which is 11 (44.0%) cases followed by primary school, SSC, HSC, and illiterate which were 6 (24.0%) cases, 4 (16.0%) cases, 3 (12.0%) cases and 1 (4.0%) case respectively. The difference between these two groups was not statistically significant (p=0.628).

Service was the main occupation of the patients of group A (terbinafine group). We found 15 (60.0%) cases in this category followed by student, housewife, business and laborers which were 5 (20.0%) cases, 2 (8.0%) cases, 2 (8.0%) cases and 1 (4.0%) case respectively. In contrast, among the patients of group B (butenafine group) majority (9, 36.0%) were students followed by service, housewife, laborers and business which were 8 (32.0%) cases, 3 (12.0%) cases, 3 (12.0%) cases and 2 (8.0%) cases respectively. The difference between these two groups was not statistically significant (p=0.345) (Table I).

Table I: Characteristics of the study participants

Characteristics	Group A (n=25) Number (%)	Group B (n=25) Number (%)	p values
Age in years			
<21	03 (12.0)	06 (24.0)	0.614[ns]
21−30	13 (52.0)	07 (28.0)	
>30	09 (36.0)	12 (48.0)	
Mean ± SD	31.88 ±11.08	30.40 ±9.51	
Sex			
Male	19 (76.0)	21 (84.0)	0.479[ns]
Female	06 (24.0)	04 (16.0)	
Marital Status			
Married	14 (56.0)	16 (64.0)	0.563[ns]
Single	11 (44.0)	09 (36.0)	
Educational Level			
Illiterate	01 (4.0)	01 (4.0)	0.628 [ns]
Primary School	03 (12.0)	06 (24.0)	
SSC	06 (24.0)	04 (16.0)	
HSC	06 (24.0)	03 (12.0)	
Graduate & above	09 (36.0)	11 (44.0)	
Occupation			
Service	15 (60.0)	08 (32.0)	0.345[ns]
House wife	02 (8.0)	03 (12.0)	
Student	05 (20.0)	09 (36.0)	
Business	02 (8.0)	02 (8.0)	
Laborers	01 (4.0)	03 (12.0)	

ns = Not significant

Baseline clinical presentation of the study participants

Most of the study participants (88%) 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 (p=1.000). In group A (terbinafine group), erythema was present in 25 (100.0%) cases, scaling was present in 25 (100.0%) cases, central clearing was present in 22 (88.0%) cases, papule was present in 23 (92.0%) cases, vesicles was present in 9 (36.0%) cases, maceration was present in 5 (20.0%) cases and pruritus was present in 25 (100.0%) cases. In group B (butenafine group), erythema was present in 24 (96.0%) cases, scaling was present in 23 (92.0%) cases, central clearing was present in 19 (76.0%) cases, papule was present in 21 (84.0%) cases, vesicles was present in 10 (40.0%) cases, maceration was present in 6 (24.0%) cases and pruritus was present in 24 (96.0%) cases, The difference was not statistically significant (p>0.05) between two groups (Table II).

Table II: Presentation of Tinea cruris among the study participants

Characteristics	Group A (n=25) Number (%)	Group B (n=25) Number (%)	p values
Number of lesions			
Multiple	22 (88.0)	22 (88.0)	1.000[ns]
Single	03 (12.0)	03 (12.0)	
Clinical findings			
Erythema	25 (100.0)	24 (96.0)	0.312[ns]
Scaling	25 (100.0)	23 (92.0)	0.148[ns]
Central Clearing	22 (88.0)	19 (76.0)	0.269[ns]
Papule	23 (92.0)	21 (84.0)	0.333[ns]
Vesicles	09 (36.0)	10 (40.0)	0.770[ns]
Maceration	05 (20.0)	06 (24.0)	0.732[ns]
Pruritus	25 (100.0)	24 (96.0)	0.500[ns]

ns= Not significant

Comparison of clinical assessment score between the groups before and after treatment

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 mean score of the two groups was significant (p=0.001) (Table III and Fig 1).

Table III: 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[ns]
After 1st week	5.72±0.7	4.12±0.7	0.001[s]
After 2nd week	3.04±0.5	1.44±0.9	0.001[s]

ns=Not significant; s= Significant

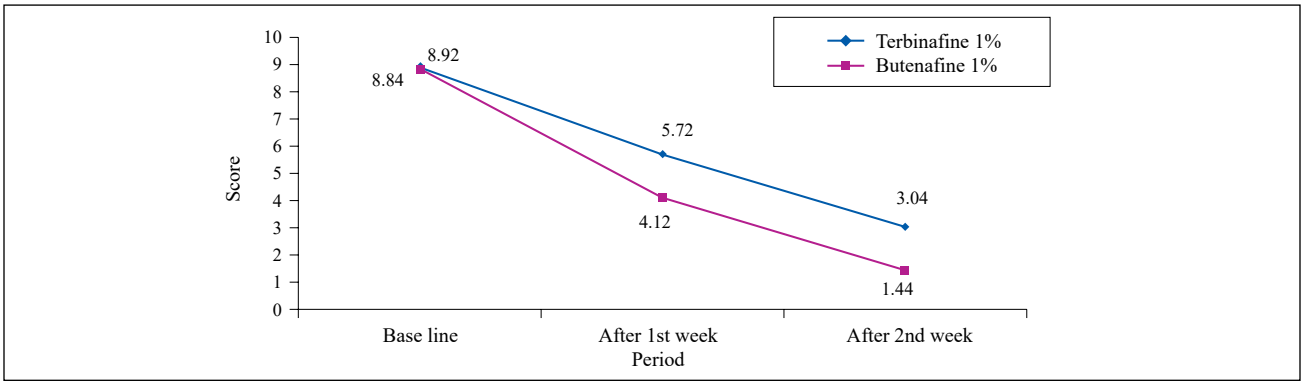

Fig 1. Line graph showing the improvements of the study patients according to clinical assessment scoring

Table IV: Comparison of adverse effects among the treatment groups

Side effect	Group A (n=25) Number (%)	Group B (n=25) Number (%)	P value
Burning			
Yes	01 (4.0)	0 (0.0)	0.500[ns]
No	24 (96.0)	25 (100.0)	

ns= not significant

Comparison of adverse effects between the groups after treatment

Transient burning sensation at the application site was found in one of 25 (4.0%) 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

Newer classes of antifungals like the allylamines and benzylamines were developed to combat the increasing incidence of resistant fungal infections as well as to produce quicker response with lesser side effects. Terbinafine and butenafine are the antifungals that represent the groups respectively and both were tested individually for their efficacy. However, there is still paucity of published evidence where their efficacy has been compared together. Under this circumstance, our current study which to the best of our knowledge was the first study in Bangladesh that compared the efficacy and safety of topical terbinafine 1% and butenafine 1% cream in the treatment of tinea cruris.

In the present study, it was observed that in group A (terbinafine group), majority of the patients (52.0%) were in their 3rd decade of life followed by more than 30 years (36.0%) and under 21 years (12.0%). In Group B (butenafine group), majority of the patients were in the age group of more than 30 years (48.0%) followed by 3rd decade and under 21 years which were 28.0% cases and 24.0% cases respectively. The mean age with SD in group A (terbinafine group) and group B (butenafine group) were 31.88±11.08 years and 30.40±9.51 years respectively, which were similar in two groups. The mean difference between the age of two groups was not statistically significant (p>0.05), which indicates that tinea cruris is predominant in 3rd decade and above. Similarly, Choudhary et al[11] showed in their study that all the patients had similar demographic features with age ranged in between 16 and 35 years in both the groups. Das et al[12] also found most of the patients' age belonged to 30−45 years accounting for 67.0% of the study group. The youngest patient was 18 years and the oldest patient was 61 years, which are consistent with the findings of our current study. On the other hand, Jerajani et al[13] and Rotta et al[14] 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.

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.[15] Similarly, in this current study it was observed that in Group A (terbinafine group) male was predominant than female which was 76.0% cases and 24.0% cases respectively. In Group B (butenafine group) males were predominant compared with females (84.0% cases and 16.0% cases respectively). The difference between these two groups was not statistically significant (p>0.05). Male to female ratio was 3.2:1 and 5.3:1 in Group A (terbinafine group) and Group B (butenafine group) respectively and 4:1 in the whole study patients. As regards to the incidence of tinea cruris, a number of other studies found male predominance (11−14), which closely resembles with the findings of the present study.

It was observed in this study that, the mean clinical assessment scoring with SD in Group A (terbinafine group) and Group B (butenafine group) were 8.92 ± 0.6 and 8.84±0.8 respectively at baseline before initiation of treatment. The difference between the mean score of two groups is not significant (p=0.690). The mean clinical assessment scoring with SD in Group A (terbinafine group) and Group B (butenafine group) were 5.72±0.7 and 4.12±0.7 respectively after 1 week of treatment. The difference between the mean score of the two groups was significant (p=0.001). The mean clinical assessment scoring 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 mean score of the two groups was significant (p=0.001). Ramam et al[9] 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[16] 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.

One single study by Das et al[12] that compared these two drugs butenafine and terbinafine in the treatment of tinea cruris showed that at the end of 42 days, the overall cure rates were 79.49% in the Regimen II (butenafine) group and 62.16% in the Regimen I (terbinafine) group. The effective treatment rates after 2 weeks of post-treatment follow-up was 92.31% in Regimen II (butenafine) and 81.08% in Regimen I (terbinafine) study group which were all statistically significant ($p<0.05$). The study concluded that treatment with butenafine 1% cream was considered superior to treatment with terbinafine 1% cream in case of tinea cruris.[12]

In this study, it was observed that burning was found in 1(4.0%) case in Group A (terbinafine group) and not found in Group B (butenafine group). The difference was not statistically significant ($p>0.05$) between two groups. Similar findings were also reported by a study of Jerajani et al[13], 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.[17]

In conclusion, results of our present study revealed that there were 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.

Strength and Limitations of the study

Although this study was important due to its unique nature of being the first study done in low-resource setting exploring the efficacy of butenafine 1% cream and terbinafine 1% cream in treatment of tinea cruris, its findings should be interpreted in light of some limitations. The first limitation was that the study population which was selected from one selected hospital of Dhaka city, so that the results of the study might not reflect the exact picture of the whole country. Moreover, the present study was conducted over a very short period of time on a small sample size which was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size and robust methodology.

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