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A Clinical Study of Efficacy and Safety of Topical Antifungal Agents for the Treatment of Tinea Corporis

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Abstract

Background: *Skin fungal is a common presentation in tropical countries like India. Tinea corporis is the name given to all dermatophytosis of glabrous skin except palms, soles, and groin. The present study was done to determine the efficacy and safety profile of topical antifungal drugs clotrimazole and sertaconazole.* ***Methods:*** *The study was conducted in the OPD of the Department of Dermatology, on patients with the diagnosis of tinea corporis. A total of n=80 cases were taken up for the study divided randomly into two groups of n=40 each. Group I used sertaconazole cream and group II clotrimazole used cream. The patients were advised to apply the drugs twice daily topically for a period of three weeks. The follow-up parameters like erythema, scaling, itching, margins, size, and KOH mounts were taken for comparison of results.* ***Results:*** *The overall reduction in the size of the lesion to grade 0 in group I was 47.5% and group II was 65.5%. the p-values were 0.0334 which were considered significant. Pre-treatment KOH mount in group I was grade 2 in 40 cases and post-treatment KOH mount investigation 95% were converted to grade 0 (KOH Negative) at the end of treatment. In group II the values of grade 2 were converted to grade 0 (KOH Negative) in all 100% cases. No significant adverse reactions were reported to cases in both groups.* ***Conclusion:*** *At the end of 4 weeks sertaconazole 2% cream showed a significant reduction in erythema, scaling, itching, and margins except for size compared to clotrimazole 2% cream. Hence, sertaconazole 2% may the choice of treatment in skin lesions of T. Corporis.*

Keywords*: Antifungal Agents, Clotrimazole, Sertaconazole, Tinea Corporis*

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Introduction

Dermatophytes are a group of related fungi that invade the skin, hairs, and nails of humans or other animals leading to a condition called dermatophytosis. [1] Dermatophytosis is a common presentation in countries like India due to tropical climate conditions. The incidence of topical fungal infections has shown to be increasing in recent years which could be because of the increased availability of better health care facilities leading to better diagnosis and treatment. Also, could be because of the increased number of people using health clubs, community swimming pools, and immunocompromised patients which favors the spread of such infections. [2] Fungal infections can be superficial, subcutaneous, or systemic. The superficial fungal infections are generally confined to corneum stratum, nail, and hairs. [3] WHO has shown that dermatophytes affect at least 25% of all populations across the world. [4] About 30-70% of adults are asymptomatic hosts for these pathogens the incidence of which shows an increase with an increase of age. T. rubrum is the cause of chronic and recurrent infections in 80 - 93% of cases. The common therapy for the disease is topical or oral

antifungal drugs. The oral antifungal agents include Fluconazole, Itraconazole, Griseofulvin, Terbinafine, Flucytosine and others. The drugs have shown poor compliance because of increased costs and length of treatment apart from gastrointestinal side effects. [3] There are reports of rapid development of resistance to flucytosine and cases of relapse are seen following treatment with itraconazole. [5] Topical antifungal agents like fluconazole, clotrimazole ciclopirox, etc. have been used. Clotrimazole is a broad-spectrum topical antifungal agent generally well tolerated however, cases with erythema, burning, peeling, blistering, edema, pruritis, and urticaria have been reported. [5, 6] Sertaconazole is a newer topical imidazole that has better antifungal activity as compared to other topical agents. [7, 8] It has shown promising results following once-daily application for up to 3 weeks. [7, 8] This study was done to evaluate the efficacy and safety of clotrimazole and setraconazole in the treatment of tinea corporis.

Materials and Methods

This cross-sectional study was carried out on OPD patients in the Department of Dermatology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study.

Inclusion criteria

1. Patients in the age group of 18 – 50 years having clinical manifestations of Tinea corporis such as erythema, scaling, vesicles, pustules, and itch.
2. Skin scrapings positive for KOH mount are included in the study.

Exclusion criteria

1. Pregnant and lactating females.
2. Hypersensitivity to azole drugs
3. Patient with systemic mycosis
4. Patients with a history of diabetes mellitus and other systemic illness

After the selection of the patients, a detailed history and clinical examination were done in good light to determine the number, the type, presence of inflammatory margins, and extent of involvement of lesions. The affected areas were cleaned with 70% alcohol swabs to remove surface contaminants. After the evaporation of alcohol, the skin scrapings were collected from the border of the lesions with a sterile scalpel blade on a sterile black paper envelope and the samples were sent to the Department of Microbiology for examination. The samples were placed in few drops of KOH 10% on a clean glass slide the coverslip was placed and gently heated by passing over the flame 3-4 times. After half an hour the specimen were looked at in low power and then high power to determine the presence of hyphae or arthrospores. The scoring was given as 0=KOH negative, 2=KOH positive. A total of n=80 patients were identified and included in the study they were randomly in two groups of n=40 each. Group I used clotrimazole cream 2% and group II sertaconazole 2% cream was used. The patients were advised to apply the drugs twice daily topically for a period of four weeks. The photograph of the lesions taken before treatment, after two weeks, and at the end of the study were used for assessing the clinical improvement of the case.

The patients were monitored for the following signs

Colour of the lesion

Change in color from erythema to normal skin color was noted. The scoring was given in the following manner. 0=Absent, 1=mild, 2=moderate, 3=severe

Scaling of the lesion: The Scoring was given in the following manner. 0=Absent, 1=Mild, 2=Moderate, 3=Severe.

Itching

The scoring was given in the following manner.0=no itching, 1=Mild itching not affecting daily activities, 2=Moderate itching affecting daily activities, 3=Severe itching disturbing the sleep.

Borders of the lesion

Whether the lesion shows progressive (presence of papules, vesicles) or regressive pattern (return to normal skin pattern). Scoring was given in the following manner: 0=Regressive, 1=Stagnant, 2=Progressive

Size of the lesion

Whether there is an increase or decrease in size. Scoring for lesion size is as follows: 0=size less

than 5cms in circumference, 1=size 5-10cms, 2=size 10-20cms,
3=size > 20cms

Statistical analysis

After collecting the raw data, the values in all the groups were analyzed by using SPSS version 19 on Windows format for descriptive and analytical statistics.

Results

The data for demographic profile, pharmacological treatment prescribed, and its effect on the clinical outcomes were collected over a period of 4 weeks and analyzed. In this study out of n=40 of group I n=25 were males and n=15 were females. The mean age of group I was 28.5 ± 3.5 years. In group II the number of males was n=22 and females were n=18 the mean age was 27.5 ± 4.5 years. The comparison of pre-and post-treatment erythema in group I showed a decrease in several cases in grade II and grade III following 4 weeks of therapy. Similarly, in group II 82.5% of cases were converted in grade 0 following treatment. The p-values at the post-treatment between group I and group II were 0.0458 which is considered significant details are given in table 1.

Table 1: Comparison of pre and post-treatment erythema in both groups

Grade	Group I			
	Pre-treatment (n)	*Percentage*	*Post-Treatment (n)*	*Percentage*
0	00	00.00	12	30.00
1	13	32.50	22	55.00
2	18	45.00	06	15.00
3	09	22.50	00	00.00
Total	40	100.0	40	100.0
Grade	**Group II**			
0	00	00.00	33	82.5
1	05	12.50	05	12.5
2	25	62.50	02	5.00
3	10	25.00	00	0.00
Total	40	100.0	40	100.0

Pre-treatment and post-treatment scaling observations found in group I found decrease in number of patients from 32.5%, 45% and 22.5% in grades 1, 2, and 3 respectively were converted to 30%, 55%, and 15% in grade 0, 1 and 2 respectively. In group II 12.5%, 62.5%, 25% in grades 1, 2, and 3 respectively were converted to 82.5%, 12.5%, 5% in grades 1, 2, and 3. P values following post treatment were 0.0122 considered significant (table 2).

Table 2: Comparison of pre and post-treatment scaling in both groups

Grade	Group I			
	Pre-treatment (n)	*Percentage*	*Post-Treatment (n)*	*Percentage*
0	00	0.00	15	37.5
1	18	45.00	25	62.5
2	20	50.00	00	0.00
3	02	5.0	00	0.00
Total	40	100.0	40	100.0
Grade	**Group II**			
0	00	0.00	27	67.5
1	05	12.5	13	32.5
2	35	87.5	00	0.00
3	00	0.00	00	0.00
Total	40	100.0	40	100.0

The comparison of pre-treatment and post-treatment itching scores revealed out of 100% cases in grades 2 and 3 were decreased to 25% and 75% in grade 0 and grade 1 following treatment with clotrimazole cream 2% (group I). In group II out of the total cases in grade 1, 2, and 3 were converted to grade 0 (75%) and 1 (25%). Post-treatment values of both groups for p-values were calculated to be 0.0324 hence considered significant depicted in table 3.

Table 3: Comparison of pre and post-treatment itching in both groups

Grade	Group I			
	Pre-treatment (n)	*Percentage*	*Post-Treatment (n)*	*Percentage*
0	00	00.00	10	25.0
1	00	00.00	30	75.0
2	35	87.5	00	0.00
3	05	12.5	00	0.00
Total	40	100.0	40	100.0
Grade	**Group II**			
0	00	00.00	30	75.0
1	05	12.5	10	25.0
2	33	82.5	00	0.00
3	02	5.0	00	0.00
Total	40	100.0	40	100.0

The patients of Group I with grade 2 margins from 80% to 20% of grade 2 and 3 pre-treatment were increased significantly from 0% to 22.5% and 77.5% in grade 0 and 1 respectively in the post-treatment period. The pre-treatment grades were reduced in group II to 12.5% and 87.5% in grade 0 and 1 respectively the corresponding p values were 0.256 hence not considered significant shown in table 4.

The overall reduction in the size of the lesion to grade 0 in group I was 47.5% and group II was 65.5%. the p-values were 0.0334 which were considered significant (table 5). Pre-treatment

KOH mount in group I was grade 2 in 40 cases and post-treatment KOH mount investigation 95% were converted to grade 0 (KOH Negative) at the end of treatment. In group II the values of grade 2 were converted to grade 0 (KOH Negative) in all 100% cases. No significant adverse reactions were reported to cases in both groups.

Table 4: Comparison of pre and post-treatment margins in both groups

Grade	Group I			
	Pre-treatment (n)	*Percentage*	*Post-Treatment (n)*	*Percentage*
0	00	00.00	09	22.5
1	00	00.00	31	77.5
2	32	80.00	00	0.00
3	08	20.00	00	0.00
Total	40	100.0	40	100.0
Grade	**Group II**			
0	00	00	05	12.5
1	03	7.5	35	87.5
2	35	87.5	00	00.00
3	02	5.0	00	00.00
Total	40	100.0	40	100.0

Table 5: Comparison of pre and post-treatment size of the lesion in both groups

Grade	Group I			
	Pre-treatment (n)	*Percentage*	*Post-Treatment (n)*	*Percentage*
0	01	2.5	19	47.5
1	15	37.5	11	27.5
2	20	50.0	08	20.0
3	04	10.0	02	5.0
Total	40	100.0	40	100.0
Grade	**Group II**			
0	00	00.0	26	65.0
1	25	62.5	14	35.0
2	10	25.0	00	00.0
3	05	12.5	00	00.0
Total	40	100.0	40	100.0

Discussion

The present cross-sectional study was done to determine the efficacy and safety of clotrimazole and sertaconazole in our tertiary care teaching institute. Patients were selected for those visiting the dermatology OPD in whom the diagnosis of tinea corporis was made based on KOH mount observations. The results show that there was no significant age difference in both the groups including the sex distribution which indicates that both groups were homogeneous as far as age and sex are concerned. The analysis of parameters in both groups for erythema, scaling, itching margins, and size in the pre-treatment category using Mann Whitney U test shows in all categories the p-values were not significant. The efficacy of topical treatment was determined by the ability of the treatment for shifting of patients from grade 2 and 3 to grade 0 which is considered normal. The analysis of table 1 showed sertaconazole 2% cream (Group II) was able to convert 67.5% into grade 0 as compared to clotrimazole 2% cream (Group I) only 37.5% were converted to grade 0. Similarly, the post-treatment size of the lesion and ability to convert KOH mount to negative was found to be greater by the sertaconazole group. The antifungal properties of sertaconazole have been evaluated in a wide range of fully published in vitro studies against dermatophytes, yeasts, and opportunistic infections of filamentous fungi and Gram-positive bacteria. [9, 10] In one of these studies, isolates of *T. rubrum* (n = 29) showed a higher sensitivity to sertaconazole (geometric MIC 0.063 mg/mL) than to bifonazole (0.267 mg/mL), fluconazole (5.58 mg/mL) and cyclopyroxolamine (0.351 mg/mL) but not to amorolfine (0.037 mg/mL) or terbinafine (0.024 mg/mL). [11] Moreover, in a comparative study of susceptibility against 250 clinical isolates of dermatophytes collected from Spanish hospitals, sertaconazole was shown to be one of the most effective of ten antifungal agents evaluated. [11] Sertaconazole showed a broad range of fungicidal activity (defined as a total absence of growth) in one study of 194 isolates of Candida spp. (0.5–4 mg/mL) after 48 hours of culture (the profile of fungicidal action was identical after 24 hrs of culture). [12] The pharmacokinetic data shows that immediately following topical application of 100mg single dose 2% sertaconazole cream on the skin of the back of 12 healthy volunteers, a mean of 88.9% of the compound was recovered on the skin surface. [13] The clinical efficacy data show that the clinical cure rate and the mycological cure rate of 2% sertaconazole cream were significantly superior to 2% miconazole when applied for a similar duration in cutaneous mycoses. [14] Fungal infections of the skin may elicit a local inflammatory response that results in irritation and itching. The anti-inflammatory properties of sertaconazole have been evaluated in both in vitro and animal studies. In human peripheral blood lymphocytes stimulated with phytohaemagglutinin, sertaconazole significantly ($p < 0.05$) reduced the release of

several proinflammatory cytokines compared with a range of other antifungal agents tested. [15] In the current study the reduction in erythema by clotrimazole was significantly better by sertaconazole group p-values (<0.05) (table 1) shows the better anti-inflammatory properties and efficacy of sertaconazole. Most azole drugs are fungistatic, which, although limits fungal cell growth, does not prevent the shedding of viable mycelial cells from the skin surface. Sertaconazole, however, has an additional fungicidal activity. In general, fungicidal drugs are preferred over fungistatic drugs for superficial dermatophyte infections because higher cure rates are achieved in shorter treatment times, thus increasing the likelihood of patient adherence and decreasing the incidence of recurrence. [16] One of the drawbacks of sertaconazole may be the cost factor but since the treatment produces better it should not be a constraint for treatment.

Conclusion

The present study evaluating the efficacy of 2% sertaconazole cream was compared with 2% clotrimazole cream applied topically for four weeks on the lesions of *T. Corporis*. At the end of 4 weeks sertaconazole 2% cream showed a significant reduction in erythema, scaling, itching and margins except size compared to clotrimazole 2% cream. Hence, sertaconazole 2% may the choice of treatment in skin lesions of *T. Corporis*.

Conflict of Interest: *None declared*
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