A STUDY OF COMPARATIVE ASSESSMENT OF THE EFFICACY & SAFETY OF SERTACONAZOLE 2% CREAM VERSUS TERBINAFINE 1% CREAM IN PATIENTS WITH DERMATOPHYTOSES OF SKIN
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ABSTRACT: BACKGROUND: Sertaconazole, a new broad spectrum fungicidal and fungistatic imidazole antifungal drug is having an added good antipruritic and anti-inflammatory action. This beneficial action of Sertaconazole provides much symptomatic relief to the patients with dermatophytic infections of the skin and thereby it improves the quality of life in these patients.
AIMS AND OBJECTIVES: To make comparative assessment of the efficacy and safety of Sertaconazole 2% cream and Terbinafine 1% cream in patients with dermatophytoses of skin.
MATERIALS AND METHODS: 40 patients with dermatophytic infections like tinea corporis, tinea cruris and tinea faciei attending the skin OPD, Government General Hospital, Anantapur were enrolled in this prospective, single blind, randomized study. Patients were randomized into two groups A & B with 20 patients in each group. In the initial ‘Treatment Phase’, group A patients received the sertaconazole nitrate 2% cream applied topically twice daily for four weeks and group B patients received the Terbinafine hydrochloride 1% cream applied topically twice daily for two weeks. In the ‘Follow-up Phase’ i.e. 2 weeks after the completion of treatment phase, all the patients in this study were assessed clinically and mycologically for the relapse of dermatophytic infections.
RESULTS: Out of the total 40 patients in this study, 97% of Sertaconazole group patients and 91% of Terbinafine group patients showed significant improvement in their signs and symptoms (pruritus, erythema, papules, vesicles, scaling and mycological cure) as compared to their baseline in the treatment phase and in the follow-up phase it was 100% in Sertaconazole group and 95% in terbinafine group. Higher number of patients showed decrease of pruritus in the Sertaconazole group (90%) as compared to the Terbinafine group (50%) (p < 0.05 Sertaconazole vs Terbinafine). Both the drugs were well tolerated and did not show recurrences by the mycological assessment.
CONCLUSION: Sertaconazole was better than terbinafine in relieving the signs and symptoms of dermatophytic infections and there is no recurrence of dermatophytic infections in all the patients who used these drugs at the end of follow up phase as per the mycological assessment.
KEYWORDS: Sertaconazole, Terbinafine, Dermatophytoses, Tinea corporis, Tinea cruris, Tinea faciei.

INTRODUCTION: Dermatophytosis is a superficial fungal infection of the skin caused by the fungi called dermatophytes. This infection is also called as tinea. Depending on the site of involvement in the body these are called as tinea corporis, tinea cruris and tinea faciei when the glabrous skin, groin or perineum and face are involved respectively. These dermatophytic
Infections are more common in the tropical countries like India due to environmental factors like heat and humidity in summer and monsoon seasons. The most common type of dermatophytoses in adults is the tinea corporis (36% - 59%), tinea cruris (12%-27%)\(^1,2\) and tinea faciei (3%).\(^3\) Clinically these dermatophytic infections are characterised by the appearance of ring shaped lesions with central healing and inflammatory features like erythema, papules, vesicles, scaling and with symptoms of itching and discomfort in the affected areas of the body. Scratching of these lesions due to severe itching in these patients may lead to secondary bacterial infection and eczematization associated with considerable morbidity which may impair the quality of life.

Among the many antifungal drugs available for the treatment of dermatophytoses imidazoles, allylamines and triazoles are the most effective drugs. Systemic antifungal drugs like terbinafine, itraconazole, fluconazole are used for severe and chronic dermatophytic infections.\(^4\) Topical antifungals are effective in localized dermatophytic infections. Among the many topical antifungal drugs, imidazole group of drugs like clotrimazole, miconazole and ketoconazole are used most commonly.\(^5\)

Sertaconazole is a new topical antifungal drug belonging to the imidazole group of antifungal drugs. Sertaconazole acts by indirectly inhibiting the synthesis of ergosterol, an essential component of fungal cell wall leading to the disruption of mycelial growth and replication. Sertaconazole at higher concentrations in skin may bind directly to the non-sterol lipids in the fungal cell wall leading to increased permeability and subsequently lysis of the mycelium. Depending on the concentration of sertaconazole, it can act as both fungistatic and fungicidal drug.\(^6\) A unique benzothioephene ring in the chemical structure of sertaconazole makes it more lipophilic so that it is retained in the stratum corneum for a prolonged period of about 48 hrs. This leads to higher mycological cure rate and lesser chances of relapse.\(^7\) Anti-inflammatory and antipruritic actions of the sertaconazole are considerably beneficial to the patients.\(^8,9,10\) Sertaconazole has excellent safety profile with few reported adverse cutaneous effects like allergic contact dermatitis, dryness, itching, eczema and skin tenderness.\(^11\)

Terbinafine is a broad spectrum fungicidal drug belonging to the allylamine group of antifungal drugs. Terbinafine acts by interfering with the biosynthesis of fungal sterol at an early stage. It also acts by inhibiting squalene epoxidation leading to the fungal intra cellular accumulation of toxic squalene thereby causing fungal cell death.\(^12\)

The present study was undertaken to know the efficacy and safety of the newer topical antifungal drug sertaconazole in comparison to the topical terbinafine in the treatment of the patients with dermatophytic infections like tinea corporis, tinea cruris and tinea faciei by the comparative clinical and mycological assessment.

**MATERIALS AND METHODS:** 40 Patients having dermatophytic infections of skin like tinea corporis, tinea cruris and tinea faciei affecting less than 20% of body skin surface area were selected among the patients attending the Dermatology OPD, Government General Hospital, Anantapur during the period from April, 2011 to September, 2011. As this study is a prospective, single blind, randomized control study, patients were randomly distributed into two groups A and B with 20 patients in each group. Inclusion criteria for selecting patients into this study are untreated patients with clinical diagnosis of tinea corporis, tinea cruris and tinea faciei having ring
shaped skin lesions affecting less than 20% of body skin surface area along with mycological confirmation of the superficial fungal infection by the KOH mount test, patients having dermatophytic infections of all age groups and both the sexes. Exclusion criteria includes the patients with subsiding dermatophytic infections due to the antifungal treatment taken by them, dermatophytic infections involving more than 20% body surface area of skin, patients having immunosuppressive disease or taking immunosuppressive drugs with dermatophytic infections, pregnant and lactating female patients with dermatophytic infections.

Clinical diagnosis of tinea corporis, tinea cruris and tinea faciei was made by the clinical examination of patients and by the confirmation of fungi by the laboratory KOH mount test in each patient selected for this study. The patients participated in the two groups of this study are having similar demographic features in respect of age (Ranged between 12 to 45 years in both the groups), sex (group A: males 12 and females 8 group B: males 13 and females 7) and duration of the disease (1 month to 3 months in both the groups). In the ‘treatment phase’ Group A patients were treated with sertaconazole nitrate 2% cream and group B patients were treated with terbinafine hydrochloride 1% cream. Patients were advised to apply the cream twice daily on affected sites for a period of 4 weeks in sertaconazole group and 2 weeks in terbinafine group. At the end of treatment phase, the efficacy of the drug was assessed and any adverse effects of the drug like local erythema, burning & stinging sensation, swelling, increased itching etc. were noted. For the clinical efficacy assessment purpose the patients in this study are graded as none (0), mild (1), moderate (2) and severe (3) according to the intensity of the presence of signs and symptoms of skin disease in each clinical parameter like itching, erythema, papules, vesicles and scaling. In the ‘follow-up phase’ i.e. 2 weeks after the treatment phase, clinical and mycological findings in each patient of both the groups were noted. Overall improvement in signs and symptoms of dermatophytoses was graded as successful treatment outcome (clinical cure + mycological cure), clinical success (symptomatic relief + clinical cure) and clinical failure (no clinical and mycological improvement). For mycological assessment purpose KOH mount test was done to detect the mycelium for the confirmation of fungal infections. Safety and tolerability of each drug is assessed by observing the presence of adverse effects of the drug at each follow up visit of the patient.

Chi square test is used as statistical method for analyzing the results of this study.

**RESULTS:** Among the two groups (group A and group B) of patients in this study, both the groups have similar demographic features in respect of age, sex and duration of the disease. (Table 1) In the clinical efficacy assessment of both the drugs in this study, each clinical parameter showed the following type of findings / results.

| Parameters      | Sertaconazole (Group A) | Terbinafine (Group B) |
|-----------------|-------------------------|-----------------------|
| No. of patients | 20                      | 20                    |
| Male/Female     | 12 / 8                  | 13 / 7                |
| Age (yrs) Mean±SD | 27.3±9.39              | 32.05±11.70           |
Weight (kgs)  
Mean±SD  53.46±12.26  55.04±10.80  
Height (cms)  
Mean±SD  158.23±6.46  160.67±7.23  

Table 1: Base line demographics of patients in this study

| Severity | Sertaconazole (n=20) | Terbinafine (n=20) |
|----------|----------------------|-------------------|
|          | Base line | End of treatment | Follow up | Base line | End of treatment | Follow up |
|          | no. (%)   | no. (%)          | no. (%)   | no. (%)   | no. (%)         | no. (%)  |
| None     | -         | 18(90)*          | 20(100)   | -         | 10(50)           | 18(90)   |
| Mild     | 3(15)     | 2(10)            | -         | 2(10)     | 9(45)           | 2(10)    |
| Moderate | 10(50)    | -                | -         | 10(50)    | 1(5)            | -        |
| Severe   | 7(35)     | -                | -         | 8(40)     | -               | -        |

Table 2: Comparison of findings regarding the pruritus in patients of both the groups in this study

*P<0.05 Sertaconazole vs Terbinafine.

Findings about pruritus: After the completion of treatment phase 90% of patients of sertaconazole group (group A) showed decrease of pruritus as compared to 50% of terbinafine group (group B). During the follow up phase 100% in sertaconazole group and 90% in terbinafine group showed absence of pruritus.(Table 2)

| Severity | Sertaconazole (n=20) | Terbinafine (n=20) |
|----------|----------------------|-------------------|
|          | Base line | End of treatment | Follow up | Base line | End of treatment | Follow up |
|          | no.(%)    | no.(%)          | no.(%)    | no.(%)    | no.(%)         | no.(%)  |
| None     | -         | 19(95)          | 20(100)   | -         | 18(90)        | 20(100) |
| Mild     | 3(15)     | 1(5.0)         | -         | 6(30)     | 2(10)         | -       |
| Moderate | 11(55)    | -               | -         | 10(50)    | -             | -       |
| Severe   | 6(30)     | -               | -         | 4(20)     | -             | -       |

Table 3: Comparison of findings regarding the erythema in patients of both the groups in this study
Findings about erythema: After the completion of treatment phase 95% of patients in sertaconazole group (group A) showed decrease in erythema as compared to 90% of terbinafine group. During the follow up phase all the patients in the both groups showed absence of erythema. (Table 3)

Findings about vesicles and scaling: 40% to 50% of patients in both the groups showed vesicles at the base line. After the completion of treatment phase and during the follow up phase, all the patients in both the groups showed absence of vesicles that was significant from base line. At base line 80% to 100% of total patients in both the groups of this study showed scaling which is of moderate to severe in amount. After the completion of treatment phase 100% in sertaconazole group as compared to 90% of terbinafine group showed absence of scaling. During the follow up phase all the patients of both the groups showed absence of scaling.

Findings of mycological assessment: At base line all the patients in both the study groups showed hyphae in KOH mount test. After the completion of treatment phase and during the follow up phase, all the patients in both the study groups showed absence of hyphae in KOH mount test.

Findings of overall score regarding the signs and symptoms of tinea infections of skin: At base line the mean overall score of signs and symptoms of tinea infection like pruritus, erythema, vesicles and scaling in sertaconazole group is 6.24 as compared to terbinafine group 6.56. After the completion of treatment phase, greater decrease in the mean overall score of signs and symptoms of tinea infection in the sertaconazole group (97%) as compared to terbinafine group (91%). At the end of follow up phase, the mean overall score of symptoms and signs of tinea infection became zero in 100% of sertaconazole group as compared to zero in 95% of terbinafine group. (Table 4)

| Parameters                | Sertaconazole (Group A) | Terbinafine (Group B) |
|---------------------------|-------------------------|-----------------------|
| Base line                 | 6.24±2.12               | 6.56±2.03             |
| End of treatment          | 0.19±0.42               | 0.59±0.75             |
| % of reduction            | 97                      | 91                    |
| End of follow-up          | 0.00                    | 0.33±0.15             |
| % of reduction            | 100                     | 95                    |

Table 4: Comparison of findings regarding the overall score of signs and symptoms of tinea infections in patients of both the groups in this study

The significant improvement in the overall score of signs and symptoms of a tinea corporis lesion over the leg on the skin near the knee joint treated with topical sertaconazole was shown as in the figure 1(a) and 1(b). The significant improvement in the overall score of signs and symptoms of a tinea faciei lesion treated with topical terbinafine over the face was shown as in the figure 2(a) and 2(b).
Figure 1a: shows tinea corporis lesion before application of topical sertaconazole 2% cream. (Before treatment)

Figure 1b: shows improvement of findings in tinea corporis lesion after the application of topical sertaconazole 2% cream for 4 weeks. (After treatment)

Figure 2a: Shows tinea faciei lesion before the application of topical terbinafine 1% cream. (Before treatment)

Figure 2b: Shows tinea faciei lesion after the application of topical terbinafine 1% cream for 2 weeks. (After treatment)

Safety Assessment: Both the topical drugs sertaconazole and terbinafine are well tolerated by the patients and did not produce significant side effects in this study.
DISCUSSION: Dermatophytic infections of skin like tinea corporis, tinea cruris and tinea faciei are very commonly seen superficial fungal infections among the patients attending the Dermatology OPD. Due to the inflammation in the tinea infections itching will be troublesome causing poor quality of life in these patients.

Due to inadequate treatment taken by the patients recurrence of the fungal infection is more common especially in the intertriginous areas of the body.

By analyzing the findings in the present study all of the patients in both the groups who have taken topical sertaconazole and topical terbinafine showed significant improvement in the signs and symptoms of tinea infections like pruritus, erythema, papules, vesicles and scaling as compared to the base line. After the completion of treatment phase, higher number of patients in sertaconzole group showed absence of pruritus (90%) and erythema (95%) as compared to terbinafine group of patients. This supports the view that sertaconazole has certain added antipruritic and anti-inflammatory properties over the other antifungals that ensures better compliance in adhering to the treatment and improved quality of life. The antipruritic and anti-inflammatory activity of sertaconazole is due to its ability to inhibit histamine and several other proinflammatory cytokines including PGE2. Clinical implication of this finding is significant as most of the tinea cruris infections are associated with candida organisms in which sertaconazole is highly potent antimycotic in comparison to other imidazole antifungal drugs in curing these infections. Significant improvement in vesiculation and scaling is seen in both the groups of patients as compared to the baseline. After the completion of treatment phase and follow up phase all the patients in both the groups showed negative mycological assessment on KOH mount test suggesting that there is no recurrence of fungal infection after the treatment. All the patients in the sertaconazole group showed successful treatment outcome (100%) as compared to terbinafine (95%). In a study done by the Sharma et al on the efficacy and tolerability of sertaconazole (2%) cream vs miconazole (1%) cream in patients having dermatophytoses of skin in which sertaconazole cream was applied to the skin lesions twice daily for 2 weeks produced 62.3% clinical cure rate and the drug showed good tolerability by the patients without causing significant side effects. But in this study after 4 weeks use of topical sertaconazole twice daily showed 100% clinical and mycological cure. Both the topical sertaconazole and topical terbinafine are well tolerated by the patients in this study and did not show significant side effects and are found to be safe.

The results of this study are dependent on the duration of the therapy. In this study the duration of the therapy with topical sertaconazole is for 4 weeks while with topical terbinafine it is for 2 weeks as per the standard regimen when comparing the efficacy and safety of sertaconazole in comparison to terbinafine.

CONCLUSION: By the analysis of the present study, sertaconazole proves to be better than terbinafine in relieving the signs and symptoms of dermatophytoses especially pruritus thereby improving the quality of life in these patients. The mycological cure was similar to both the sertaconazole and terbinafine treated group of patients. The mean percentage in reduction of overall signs and symptoms score in tinea corporis, tinea cruris and tinea faciei treated by sertaconazole (97%) is higher compared to the terbinafine (91%) at the end of treatment phase. Both the sertaconazole and terbinafine showed good safety and tolerability.
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