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A Comparative Study of Clinical Outcome of Use of Topical 2% Sertaconazole Versus 1% Terbinafineas Monotherapy in the Treatment of Tinea Corporis

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ABSTRACT
Tinea corporis, a superficial fungal infection caused by dermatophytes is highly prevalent in India. This condition primarily affects the limbs and the trunk and can severely impair the quality of life of the patient.
Aim: *To compare the outcome of use of Terbinafine and Sertaconazole as monotherapy in the treatment of tinea corporis.*
Materials and Methods: *58 patients were enrolled in this single blind parallel therapeutic trial.The patients were allocated to each arm of the study by stratified random sampling. Group A received treatment with Sertaconazole nitrate 2 % cream while group B received treatment with terbinafine hydrochloride 1% cream twice daily. The patients were reviewed weekly for 4 weeks and followed up for 2 weeks after completion of treatment. The primary outcome measures were percentage of patients showing clinical and mycological cure while mean improvement in clinical score was a secondary outcome measure.*
Results: *50 patients out of 58 completed the study,25 in each arm. Between the two arms, more percentage of patients in the Sertaconazole arm showed mycological clearance at weeks 2 and 3(48 and 76%) compared to Terbinafine (28 & 68%) respectively. A significantly larger number of patients in the Sertaconazole arm showed complete or near complete improvement in clinical scores(84%) at week 3 compared to those in the Terbinafine arm (68%). The mean improvement in clinical scores was significantly higher for the patients in the Sertaconazole arm at weeks 2 and 3.*
Conclusion: *Sertaconazole showed faster mycological clearance and could achieve better percentage of clinical cure in a shorter duration when compared to terbinafine.*
KEYWORDS: *Sertaconazole, Terbinafine, tinea corporis, topical antifungals, monotherapy.*

INTRODUCTION

Dermatophytes are keratinophilic organisms, which are true superficial pathogens of the human skin. Dermatophyte infections affect 20-25% of the world's population[1]and are caused by three species of dermatophytes namely Trichophyton, Epidermophyton and Microsporum.[2]These organisms produce keratinases, which aid in penetration of the superficial layers of the skin.They are mostly confined to the cornified layers of the skin. Infection by these organisms is commonly referred to as ringworm or tinea,a name which was given owing to the annular nature of the lesions. Tinea corporis is defined as ringworm affecting glabrous skin and commonly involves the limbs and the trunk. In Indian studies, tinea corporis was the most common dermatophytosis accounting for 27,34.5% and 39.1%of all cases.[3,4,5] Hot and humid climate, dampclothes, overcrowding and poor personal hygiene are all causes of the high prevalence of this condition in tropical climates.[6]

Topical antifungals are the first line of treatment in limited tinea corporis of recent onset.[7] Azoles and allylamines are the two most commonly used groups of topical antifungals. Among the azoles, the imidazole antifungals are widely used and among the allylamines, Terbinafine is most commonly used. Sertaconazole is a newer Imidazole antifungal agent with anti bacterial and anti-inflammatory properties. They are both highly effective due to their lipophilicity and have good safety profiles. [8]Though Terbinafine was considered to be the gold standard for antifungals due to its broad spectrum and quick action, [9] recent studies have shown that 2% Sertaconazole nitrate has similar activity particularly against dermatophytes.[10]

AIM OF THE STUDY

This study aims to compare the clinical outcomes of the use of 2% Sertaconazole Nitrate cream and 1% Terbinafine Hydrochloride creamas monotherapy in the treatment of Tinea corporis in 50 patients attending the OPD of a tertiary care hospital in Moinabad,Telangana.

OBJECTIVES

To compare the clinical and mycological cure rates and side effect profiles of 2% Sertaconazole nitrate and 1 % Terbinafine hydrochloride cream as monotherapy in 50 patients suffering from tinea corporis.

METHODS

Study Design

This is a prospective single blind parallel therapeutic trial in which patients suffering from tinea corporis were allocated into two treatment arms, Group A and Group B. This allocation was done by stratified random sampling. The study was presented before the institutional ethics committee and ethical clearance was received prior to the beginning.

Participants

Patients presenting to the Dermatology OPD were recruited into the study over a period of 6 months from January 2016 to June 2016. Written informed consent was taken from all the patients and any queries they expressed were answered in their own language. In case of minors, informed consent was taken from parents or guardians.

Inclusion criteria:

Patients of all ages and both sexes presenting with

1. Tinea corporis involving less than 20% of the body surface area
2. Tinea corporis involving only one body site
3. In patients with more than one lesion, patients with the largest lesion being less than or equal to10 cm

Exclusion criteria:

1. Patients who were unwilling to participate in the study.
2. Patients who were diabetic
3. Patinets who were HIV positive
4. Immunocompromised patients.
5. Patients with lesions involving more than 20% of the body surface area

6. Patients with plaques > 10 cm in diameter
7. Patients who had used topical/systemic antifungals three months prior to the study
8. Patients with history of use of topical or systemic glucocorticoids.
9. Pregnant or lactating women.

Setting and duration

The data was collected and recorded in the OPD from January 2016 to June 2016.

Intervention:

Following recruitment and informed consent, a thorough clinical history was taken and clinical evaluation was done. The patients were evaluated based on severity of itching, erythema and scaling. A score was given for each category ranging from 0 to 4 with zero indicating absence and 4 standing for very severe and this score was recorded for each patient (Table 1). KOH mount was done for each patient on recruitment and was repeated at weeks 1,2,3 and 4. The patients were allotted to each treatment arm by stratified random allotment. 29 patients were treated with 2% Sertaconazole nitrate cream (Group A) while 29 patients received 1% Terbinafine hydrochloridecream (Group B).The patient was unaware of which treatment arm he/she was allotted to.

Each patient was given a sufficient amount of the preparation for 4 weeks and was advised to use the preparation twice daily for the study period. The patients were followed up at weeks 1,2,3 and 4.At each week, evaluation of the symptoms and signs was done and the clinical score was noted, following which 10% KOH mount was repeated. The improvement in clinical scores was recorded at each visit and the percentage of improvement was also noted. At each visit, patients were questioned about the presence of any new lesions, sensations like burning, stinging and worsening of itch to rule out adverse effects due to the preparations.

Outcome Measures

Clinical cure was defined as percentage of patients showing complete (100%) or near complete(75%) improvement in signs and symptoms while mycological cure was defined as negative KOH mount. The primary outcome measures were clinical and mycological cure (75 to 100% improvement in symptom scores and KOH negativity) while secondary outcome measure was mean improvement in clinical scores.

Sample Size

The sample size was calculated based on previous studies and the prevalence of the condition.A total of 58 patients were recruited into the study.

Statistical Methods

The outcome measures were analyzed by unpaired T test with a confidence interval of 95%.A p value of less than 0.05 was considered significant. Mycological cure was assessed by means of Chi square test. Statistical analysis was done using SPSS software version 21.

RESULTS

Participant flow

50 patients completed the study while 8 were lost to follow up,4 in Group A and 4 in Group B. Thus each arm of the study comprised of 25 patients. None of the patients reported adverse effects and treatment was continued uninterrupted for 4 weeks with a follow up period of 2 weeks. The recruitment was completed after the desired sample size was reached. The trial was completed when all the patients had completed 4 weeks of treatment and 2 weeks of follow up.

Baseline data

Of the study population, 32 were male and 18were female. (Table 2). The youngest patient was 5 years old while the oldest was 56 years old.The mean age of the study population was 30.06 yrs. The mean clinical score for group A was 10.92 and the mean initial score for group B was 10.36.There was no statistically significant difference in clinical scores between the two groups.

Outcomes

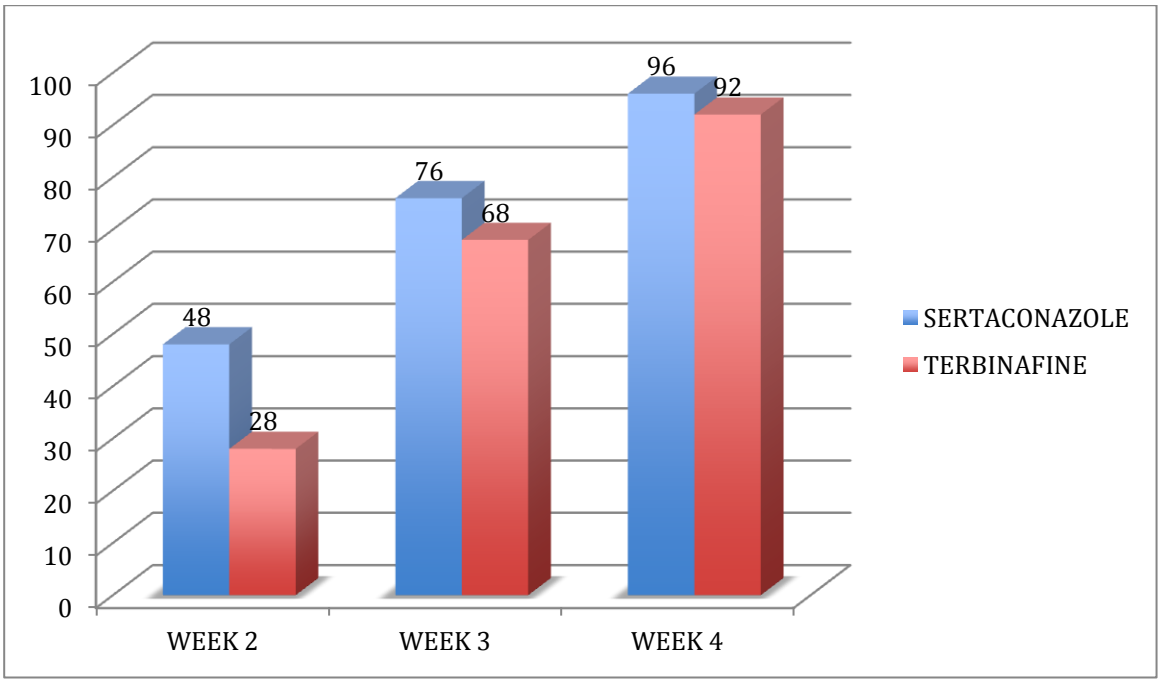
47 patients (94%) out of 50 showed complete or near complete resolution of the lesions on completion of the study period. Mycological cure was achieved in 48,76 and 96% of patients in Group A at weeks 2,3 and 4 respectively. The

same was achieved in 28,68and 92 % of patients in Group B at weeks 2,3 and 4. (Graph 1)

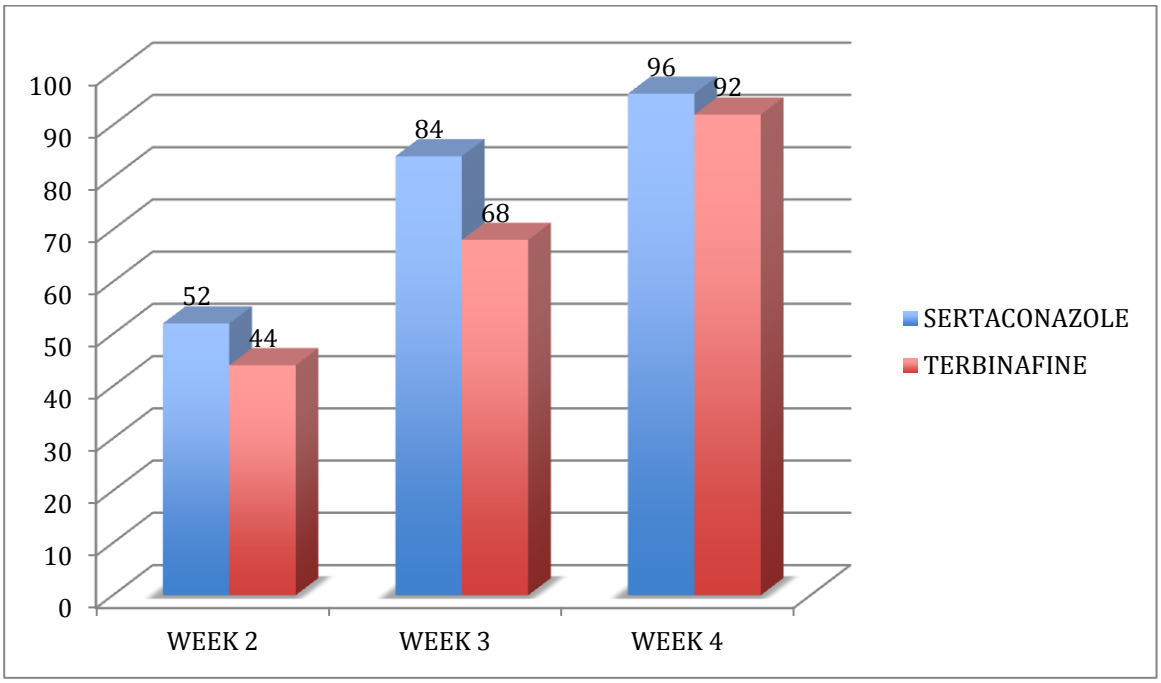
At week 1,Group A and B showed 25% improvement in clinicalscores in 52% and 56 % of patients respectively while 50 % improvement in scores was seen in 48%and 44% of patients respectively. At week 2, 50 % improvement in clinical scores was seenin 48 % of patients in Group A.52%patients in Group A experienced 75% reduction in clinical scores by week 2 while 44% patients in Group B experienced the same. This was statistically significant (p value<0.001).84% in Group A experienced complete or near complete relief of symptoms at week 3 while 68% in Group B experienced the same.4% and 8% of patients in each arm experienced 25 % relief in symptoms at week 3.12% and 16% in each arm experienced 50% reduction in symptoms by week3. This difference was statistically significant (p<0.001). By week 4,96% of patients in Group A and 92 % of patients in Group B experienced complete (100%) or near complete (75%) improvement in symptom scores. (Graph 2)

The mean improvement in scores for Group A at weeks 1,2,3 and 4 was 2.88 and that of group B was 2.72.This was not statistically significant. However the mean improvement in scores for Group Aat week 2 was 6.04 and that of Group B was 5.44.t test was 1.82 with a degree of freedom of 48.p value was 0.03749.This is statistically significant. Similarly the means at week 3 were 8.92 and 8.08.Their difference was statistically significant. t test value 2.37 with a degree of freedom of 48.p value 0.010927.At week 4,the mean improvement in scores for groups a and b was 10.36 and 9.96 respectively. This improvement was not statistically significant. (Table 3)

During the follow up period of 4 weeks, there was no recurrence seen in patients of either treatment arm.



Graph I: Percentage of patients showing mycological cure at weeks 2,3 and 4 in each study arm



Graph II: Percentage of patients showing clinical cure at weeks 2,3 and 4 in each study arm.

DISCUSSION

Sertaconazole is an azole antifungal introduced to the market in 2003.It is relatively more lipophilic than the other azole antifungals and hence can accumulate in the stratum corneum in higher concentrations.Like other azole antifungals it inhibits the enzyme Lanosterol 14 alpha demethylase which catalyses the conversion of lanosterol to ergosterol. It also leads to altered membrane permeability and leakage of intracellular contents in the organism by binding to non steroid cell membrane lipids. It can be fungistatic or fungicidal depending upon the concentration .It also has antibacterial action. Allergic contact dermatitis is a rare side effect of this otherwise safe antifungal agent.

Terbinafine has 80-90% clinical and mycological cure rate for the treatment of tinea corporis and tinea cruris. It is a broad-spectrum antifungal belonging to the allylamine group and has both fungistatic and fungicidal properties.It is highly lipophilic and can achieve high concentrations in stratum corneum,sebum and hair follicles. Thus the chance of recurrence is reduced. It can achieve high tissue concentrations within 1 week of topical application and acts by decreasing ergosterol synthesis by squalene epoxidase inhibition. Terbinafine has very few side effects,pruritus and Allergic contact dermatitis among them.

Sertaconazole was found to be more effective than placebo and more effective than Clotrimazole in a previous study by Sharma et al.[11]Similarly terbinafine was found to be more effective than azole antifungals in previous studies.[12]

In our study, both agents showed good safety profiles with no adverse effects noted in either arm. This trend is similar to that seen in previous studies. In a Japanese study by Kagawa et al,only 6 patients out of 629 treated with topical Terbinafine experienced side effects.[13]

At week 1, both agents showed similar mean improvement in scores and similar number of patients showing 25 to 50% improvement in clinical scores.KOH mount negativity was not seen in patients in either arm of the study at week 1.Similar results were seen in the study by Choudhary et al.[14]

At week 2, a significantly higher percentage of patients on Sertaconazole experienced 50 to 75 % improvement in symptom scores. This is similar to previous studies where Sertaconazole led to better improvement in symptom scores.[14]However the KOH mounts were negative in 48 % of

patients on Sertaconazole by week 2, a figure nearly double that of Terbinafine indicating faster mycological clearance. This shows that Sertaconazole also achieves desired tissue concentrations by week 2.The mean improvement in clinical scores interestingly is higher for Sertaconazole than for terbinafine at week 2 and this difference was statistically significant.

At week 3,76% of patients on Sertaconazole experienced mycological cure as compared to 68% of the patients on terbinafine.The mean improvement in scores at week 3 was also significantly higher for patients treated with sertaconazole.84% of patients on Sertaconazole experienced clinical cure as compared to 68% of patients on Terbinafine, a difference that was statistically significant. This indicates faster improvement in clinical scores. Both agents showed similar mycological clearance rates and clinical cure rates at week 4.

However Sertaconazole shows mycological clearance rate and clinical cure rates in higher percentage of people by the end of weeks 2 and 3 whereas terbinafine achieves similar rates following an additional week of treatment.This trend is similar to the one seen in studies by Selvan et al[15] and Sumitha et al.[16]

The symptomatic improvement in patients on Sertaconazole is also much higher than terbinafine at weeks 2 and 3 as evidenced by the difference in mean clinical scores.Similar trends are emerging in recent studies.[17]

CONCLUSION

As monotherapy, Sertaconazole shows faster mycological clearance and better clinical improvement in a shorter period of use when compared to terbinafine in limited tinea corporis. Both the drugs are very safe as evidenced by the complete absence of adverse effects among patients using it in our study.

SOURCES OF SUPPORT: NIL

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