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Original Research Article

Topical Amorolfine, Luliconazole, Sertaconazole and Terbinafine Effectiveness in Tinea Corporis and Tinea Cruris: A Comparative Study

Iftekhar Khan

Associate Professor, Department of Skin and VD, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.

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Corresponding author: Dr. Iftekhar Khan
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Abstract

Aim: The main aim of the study is to compare the efficacy of newer antifungals like Luliconazole, Amorolfine, sertaconazole and terbinafine cutaneous mycoses. The study also aims to evaluate the effectiveness and safety of these newer topical antifungals. **Materials and Methods**: It is a Prospective parallel study and a randomized comparative study done at Department of Skin and VD, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar to evaluate the efficacy of newer antifungal drugs. Study population as a total 300 patients, needed to be enrolled in the study based on the inclusion and exclusion criteria. All the patients are aged between 18 to 70 years. Patients will receive the newer antifungals randomly and the test product needed be applied once daily for 1 week in patients with Tinea cruris/ Tinea corporis. Follow up as the first follow up will be at 1 week and all the patients will be evaluated for clinical parameters and global clinical response. The second follow up is at 4 weeks and all the patients are again needed to the assessed for the parameters. Adverse events were recorded at each visit. **Results**: A study population included 186 (62.0%) male patients and 114 (38.0%) female patients, the youngest patient was 18 years and the oldest was 69 years. The efficacy was higher in Sertaconazole (93.3%) group followed by Luliconazole, Amorolfine, Terbinafine. **Conclusion**: The efficacy was higher in Sertaconazole (93.3%) group followed by Luliconazole, Amorolfine and Terbinafine. And the Adverse events order as follows Luliconazole >Terbinafine >Amorolfine >Sertaconazole.

Keywords: Tinea corporis, Sertaconazole, antifungals

Introduction

Tinea is superficial fungal infections typically caused by dermatophytes Common pathogens include *Trichophyton rubrum, Trichophyton mentagrophytes*, and *Epidermophyton floccosum* [1]. Superficial fungal infections are widespread, with an estimated worldwide prevalence of 20%–25%, and include tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm), among others [2]. Tinea of the skin presents clinically as well-demarcated, scaling, and inflamed lesions, which are often accompanied by an itching or burning sensation [3]. In the case of tinea pedis, maceration and vesiculation may also be present.

Infection is generally limited to the superficial layers of the epidermis, particularly the stratum corneum and the high keratin concentration containing appendageal structures, namely hair and nails. Tinea corporis and tinea cruris refer to the dermatophytic infections of the glaborous skin of the body (excluding palms and soles) and groins respectively. Topical antifungals are exclusively used for localized lesions of dermatophytosis. Amorolfine, luliconazole, sertaconazole and terbinafine are relatively newer molecules which seem to have certain advantages over the older molecules.

Topical daily antifungal therapy is considered generally as the first line therapy for dermatophytosis owing to their high efficacy and low potential for side effects. Terbinafine is a fungicidal allylamine that inhibits squalene epoxidase that results in intracellular accumulation of toxic squalene and causes fungal cell death. Luliconazole and sertaconazole are azoles antifungals that block lanosterol 14-α demethylase which prevents the formation of ergosterol [4]. Luliconazole is a novel imidazole antifungal and is uniquely characterized by its R-enantiomer side chain in addition to one chiral center. The addition of an imidazole moiety into the ketene dithioacetate structure of the compound augments its ability to target filamentous fungi [5].

Sertaconazole has fungistatic and fungicidal mechanism by indirect inhibition of ergosterol synthesis and direct inhibition of non sterol component of fungal cell membrane leading to rapid leakage of key intracellular components and immediate cell death. It also mediates its anti-itch effects by increasing prostaglandin D2 levels in mast cells and macrophages through induction of the p38 mitogen-activated protein kinase pathway [6, 7] Amorolfine, a morpholine derivative, is the first of a new class of antifungal drugs. The mechanism of action is inhibition of ergosterol biosynthesis in the fungal cell membrane by blocking enzymes delta 14 reductase and delta 7-8 isomerase [8].

Material and Methods:

This study was designed as an observational randomized controlled clinical trial and conducted in the dermatology and VD outpatient department, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, for 1 year. Permission was taken from the institutional ethics committee before commencement.

Clinically diagnosed healthy adult patients with tinea corporis and tinea cruris requiring topical antifungal therapy were selected for the study. Location of lesion, morphology and symptoms were noted. Scrapings from the edge and/or from the scaly area of the lesions were taken. Potassium hydroxide mount (KOH Mount) followed by direct microscopy was undertaken at the beginning of treatment to confirm the diagnosis but not repeated at the end of treatment since clinical improvement rather than a cure was the primary objective of the study.

Consecutive eligible patients were prescribed topical amorolfine (0.25%), luliconazole (1%), sertaconazole (2%) and terbinafine (1%) in a serial order. Same brand of the topical drug was used throughout the period of study. Amorolfine and luliconazole were advised once daily while sertaconazole and terbinafine was twice daily application. They were asked to apply as a thin layer directly to the lesions and also a small area beyond the lesions. Response to treatment was assessed after 3 weeks with no follow-up visit. We evaluated the improvement in the pruritus, erythema and scaling with score 0 for no improvement, score 1 for partial improvement and score 2 for complete improvement.

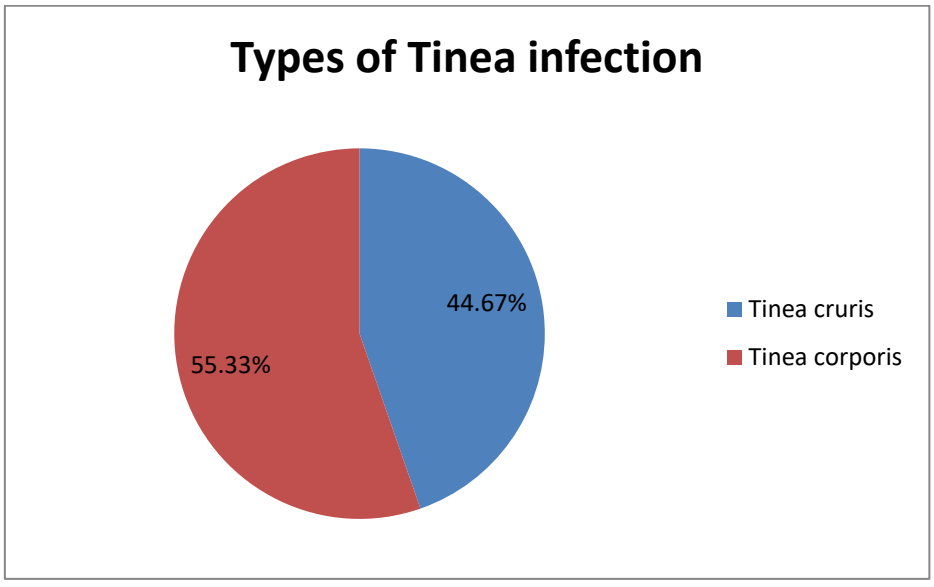
Results

Baseline demographics and disease characteristics of the patients included in this study results represented as in total 150 patients were included into the study population, divided into five groups of 30 patients and received Terbinafine(A), Luliconazole(B), Sertaconazole (C), Amorolfine (D) and compared five symptoms which were Erythema, Desquamation, Pruritus, Vesicles, and Encrustation. A study population included 186 (62.0%) male patients and 114 (38.0%) female patients, the youngest patient was 18 years and the oldest was 69 years.

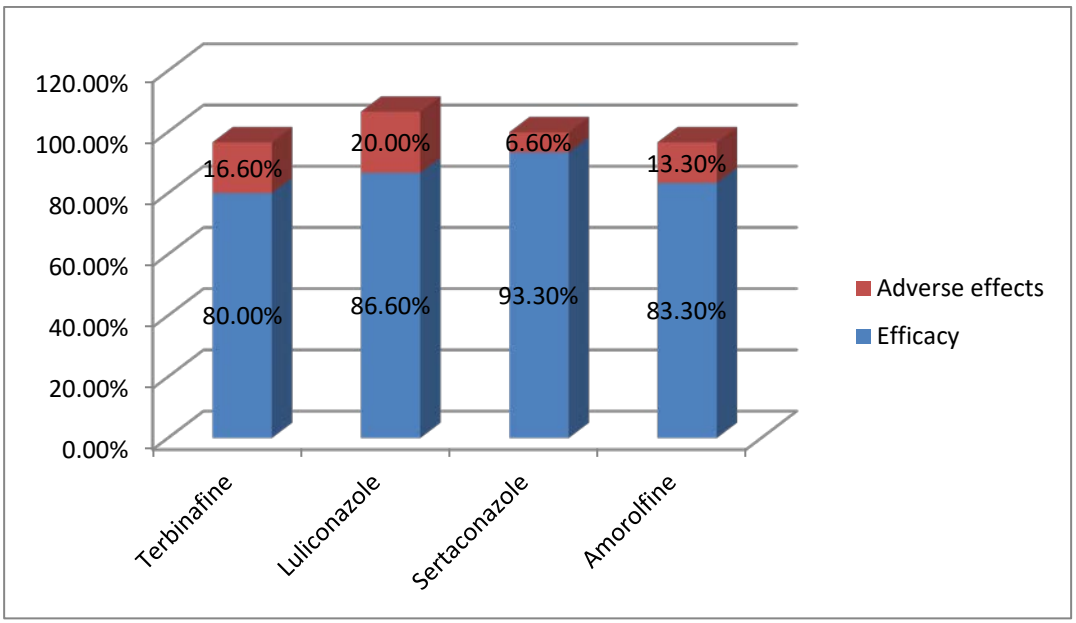
Table 1: Result

Variable		Number	%
Gender	Male	186	62.00
	Female	114	38.00
Type of infection	T. corporis	166	55.33
	T. cruris	134	44.67

The mean changes in signs and symptoms at each week in different drug treatment groups that is Amorolfine group (D), the mean changes for Erythema, Desquamation, Pruritus, Vesicles, and Encrustation were 0.74±0.71, 1.02±0.75, 0.75±0.53, 0.22±0.38 and 0.09±0.16 respectively. In Sertaconazole group (C), the mean changes for Erythema, Desquamation, Pruritus, Vesicles and Encrustation were 0.67±0.78, 0.93±0.8, 0.74±0.69, 0.20±0.39 and 0.06±0.13 respectively. In Luliconazole group (B), the mean changes for Erythema, Desquamation, Pruritus, Vesicles and Encrustation were 0.78±0.72, 0.93±0.69, 0.77±0.62, 0.19±0.35 and 0.08±0.16 respectively. In Terbinfine group (A), the mean changes for Erythema, Desquamation, Pruritus, Vesicles and Encrustation were 0.79±0.68, 1.08±0.64, 0.84±0.58, 0.22±0.29 and 0.05±0.09 respectively. The efficacy is assessed by the number of patients who has maximum improvement in signs and symptoms and those who has complete cure and the results were presented. Safety is assessed by the number of adverse events and the results were presented in Figure.



Graph 1: Types of Tinea infection



Graph 2: Different drugs adverse effects and efficacy

Discussion:

We found that the topical antifungals were effective in majority of the patients, although variable response was seen. Best response at the end of 3 weeks of topical therapy was shown by luliconazole for all three parameters pruritus, erythema and scaling, and the results were statistically significant. Jerajani et al conducted almost a similar study and found sertaconazole exhibiting better response than luliconazole and terbinafine [6]. Another study conducted by Choudhary et al showed equal efficacy between sertaconazole and terbinafine [9].

All the drugs were well tolerated, but Sertaconazole proved to be significantly more effective in terms of clinical improvement and in the eradication of fungal pathogens. In the present study Sertaconazole is having higher clinical symptom cure with 93.3%, in a study of Sharma et al.[10], 2009 & 2011 comparing sertaconazole with miconazole, Sertaconazole showed 62.3% of clinical cure ($P < 0.05$) compared with 44.6% in miconazole users. Luliconazole is having clinical symptom cure of 86.6% there is no much percentage difference compared to a previous study with different concentrations like 0.5%, 1% and 0.1% the rates of improvement in skin lesions were 90.5%, 91.0% and 95.8%, respectively showing greater efficacy rates. (Watanabe et al, 2007) In a study comparing Amorolfine and terbinafine, the Amorolfine-terbinafine combination showed higher response compared with the terbinafine group (66.7% vs. 53.5%, respectively < 0.04).[11]

In the present study Amorolfine and Terbinafine is having clinical symptom cure percentage of 83.3% and 80%. According to the results of (Sudip das et al., 2010; Bonifaz et al., 2000) Adverse events reported were mild and did not report in the discontinuation of the drug.[12] In the present study the adverse event reported with Sertaconazole was 6.6% which was very mild (Carrillo-Munoz et al., 2005). In a study of palacio et al., 1992, with Amorolfine the adverse event reporting was 13% which was comparable to that of present study which resulted in 13.3%.[13-14]

Conclusion

The efficacy was higher in Sertaconazole (93.3%) group followed by Luliconazole, Amorolfine, Terbinafine. This study also signifies the role of topical antifungal alone in treating limited tinea corporis and cruris,

thus boosting the confidence on topical therapy. Newer topical anifungals are more expensive and hence pharmaco-economical analysis should also be considered while prescribing those. Hence topical antifungals are the integral part of management of the tinea infections.

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