Journal of Pakistan Association of Dermatologists 2011; **21 (4)**: 281-284.

Original Article

Efficacy of terbinafine vs. griseofulvin in tinea capitis in the Northern areas of Pakistan

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Abstract

Background: Since longtime griseofulvin has been in use to treat tinea capitis. However due to its decreasing efficacy, higher doses and side effects a search is going on to find out a better treatment alternative. Terbinafine is one such therapeutic option.

Objectives To compare the efficacy and safety of terbinafine and griseofulvin in tinea capitis in Northern Areas of Pakistan.

Patients and methods Children 3 to 12 year-old who were clinically diagnosed for tinea capitis and confirmed by potassium hydroxide microscopy were included in the study. One group was treated with terbinafine at a dose of 62.5mg for children weighing less than 20kg and 125mg for those weighing 20-40kg and other group with griseofulvin at a dose of 15mg/kg body weight. Both groups were treated for a period of 4 weeks. Visits were scheduled at baseline and week 2, 4 and 6 for evaluation of efficacy and safety monitoring. Efficacy was evaluated on the basis of clinical improvement and mycological cure.

Results Terbinafine showed comparatively higher clinical cure in our patients as compared to griseofulvin at week 2 (35% vs. 22%), week 4 (50% vs. 38%) and week 6 (70% vs. 55%) [$p<0.05$]. Similarly, mycologic cure with terbinafine was better than griseofulvin at week 2 (30% vs. 20%), week 4 (45% vs. 35%) and week 6 (60% vs. 50%) [$p<0.05$]. *Trichophyton tonsurans* was the most common organism isolated. There were no major side effects except nausea and abdominal pain in either group.

Conclusion Terbinafine is more effective than griseofulvin in treating tinea capitis in our part of the world.

Key words
Terbinafine, griseofulvin, tinea capitis.

Introduction

Tinea capitis occurs mainly in children. Its clinical presentation varies from seborrhoeic dermatitis-like and non-inflammatory presentation like alopecia areata to severe forms like kerion with purulent discharge and secondary bacterial infection leading to scarring alopecia.[1,2] Tinea capitis is commonly caused by dermatophyte fungi *Trichophyton* and *Microsporum.*[3] However causative organisms vary from country to country.[3] Moreover migratory phenomena, changing life styles and decades of griseofulvin use have led to the change in the existing fungal species in various developed countries.[4,7,9] Present and past treatment recommendations clearly demonstrate tolerance to griseofulvin by different fungal species. In 1974 a dose of griseofulvin

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(10mg/kg/day for 4 weeks) was sufficient for the treatment of most cases of tinea capitis.[5] But nowadays off label dose of 20-25mg/kg/day for 6-8 weeks is needed to effectively treat this condition.[2] But response to griseofulvin continues to wane despite higher doses. Presently response rate was noted to be 60% compared to 80% to 90% response rate in previous studies.[6,7] This has led for a need to identify other safe and effective treatment alternatives.

Terbinafine is one such therapeutic option. Many reviews support its use in the treatment of tinea capitis.[2-5] In the Northern areas of Pakistan, there are few studies conducted to determine the best possible treatment for tinea capitis. This present study was designed to know whether terbinafine or griseofulvin is better drug for treatment of tinea capitis patients in our part of the country.

Patients and methods

It was a randomized, third party blind, single centre study. It was conducted in the Department of Dermatology Lady Reading Hospital, Peshawar and cases were enrolled from Dermatology Department Hayat Abad Medical Complex, Peshawar as well. Enrolment period extended over a period of 10 months. One hundred twenty patients were randomly allocated to two groups of 60 each. Males and females between the ages of 3 and 12 years with potassium hydroxide preparation positive for fungal elements on direct microscopy were included in the study. Patients with negative baseline KOH preparation, patients having kerion and those having treatment with topical antifungal agents within past 2 weeks or systemic antifungal agents within past 30 days were excluded from the study. Also patients with elevated liver enzymes and history of active liver disease were not included in the study. Diagnosis was based on clinical features, KOH preparation (20% freshly prepared) and culture on Sabouraud's agar. Fungal cultures were performed at Khyber Medical College Peshawar and positive dermatophyte species were identified.

Subjects were randomly allocated to one of the two groups. One group was treated with terbinafine at a dose of 62.5mg for children weighing less than 20kg and 125mg for those weighing 20-40kg and other group with griseofulvin at a dose of 15mg/kg body weight. Patients were instructed to take their medications with meals. Both groups were treated for a period of 4 weeks. Visits were scheduled at baseline visit and week 2, 4 and 6 for evaluation of efficacy and safety monitoring. Patients were examined clinically, inquired about any side effects, skin scrapings/hair were taken for mycology and blood samples drawn for hematological and biochemical profile.

Efficacy and safety evaluation

Efficacy variables included: 1. Clinical outcome based on the reduction in the severity of clinical signs and symptoms i.e. itching, erythema, scaling, area, presence of hair loss or breakage etc. 2. Mycological outcome based on fungal culture. 3. Mycological outcomes were assessed at weeks 2, 4 and 6 and scored as positive or negative.

Statistical analysis

A sample size of 60 each was estimated sufficient to detect difference between two groups. Statistical analysis was done using Chi square test. *p* value less than 0.05 was taken as significant.

Results

Overall 120 patients 3 to 12 years old were selected for the study. Out of these, 90 patients were males and 30 females. All enrolled patients completed the study.

Mycological outcome

Trichophyton tonsurans and *Microsporum canis* were the predominant dermatophytes isolated at the baseline visit, accounting for 75% and 22% respectively. Other species included *T. violaceum, T. mentagrophytes* and *M. gypseum*. A trend towards increasing negative cultures was observed with treatment. The percentage of patients with negative cultures in terbinafine group was greater than griseofulvin group (**Table 1**). Statistically this difference was significant at weeks 2, 4 and 6 ($p<0.05$).

Clinical outcome

A higher percentage of patients in terbinafine group showed clinical improvement at week 2, 4 and 6 as compared to griseofulvin group (**Table 2**). This difference was statistically significant ($p<0.05$). This shows that terbinafine produced better therapeutic response than griseofulvin in our patients.

Safety evaluation

It was comparable between two groups with none of the patients showing serious side effects apart from nausea and mild abdominal discomfort.

Table 1 Mycological cure of patients with terbinafine and griseofulvin.

Time of visit (week)	*Griseofulvin N (%)*	*Terbinafine N (%)*
2	20 (12)	30 (18)
4	35 (21)	45 (27)
6	50 (30)	60 (36)

Table 2 Clinical cure of patients with terbinafine and griseofulvin.

Time of visit (week)	*Griseofulvin N (%)*	*Terbinafine N (%)*
2	22 (13)	35 (21)
4	38 (23)	50 (30)
6	55 (33)	70 (42)

Discussion

Griseofulvin was isolated from the mould *Penicillin griseofulvum* in 1939 and was found to be effective in the treatment of human dermatophyte infections. The currently recommended dose of griseofulvin is 10-15 mg/kg/day. *Microsporum audouinii* and *M. canis* were the predominant pathogens causing tinea capitis and the use of griseofulvin led to drastic reduction in their incidence owing to their exquisite sensitivity to griseofulvin. But their decreased incidence has led to reciprocal increase in the incidence of *T. tonsurans* in some countries such as United States.[5] In our study, standard dose of griseofulvin led to mycological cure of 50% compared to 60% cure for terbinafine at 6 weeks since commencement of treatment for the two groups. This is in accordance with the previous studies for terbinafine which reported 61% to 86% cure rate with terbinafine.[9] The reason for this similarity could be that in our study Trichophyton tonsurans was the major causative organism. In the referred study as well *Trichophyton* species was the major species. Thus organisms of *Trichophyton* species might be more susceptible to terbinafine. However, mycologic cure rates with griseofulvin have previously been reported to be 62% to 92% as compared to 50% observed

in our study.[9] This could be explained by the fact that resistance might have been developing against griseofulvin leading to decreasing response to griseofulvin. Our study indicates that griseofulvin provides optimal mycological and clinical cure rates. Clinical cure based on decreasing erythema, scaling and regrowth of hair was also better with terbinafine as compared to griseofulvin. This observation was also in accordance with previously conducted studies by Friedlander[5] and Elweski *et al*.[9]

In conclusion systemic therapy with terbinafine compared to griseofulvin provided better mycological and clinical cure rates in our patients having tinea capitis. Also having low side effect profile, terbinafine, is safer as compared to griseofulvin.

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