e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(10); 680-683

Original Research Article

Efficacy and Safety of Oral Griseofulvin versus Oral Terbinafine in Pediatrics Patients with Tinea Capitis: A Comparative Study

Ranjit Debbarma[1], Mrigendra Kumar[2], Jeetendra Kumar[3]

[1]PGT (Final Year), Department of Pharmacology, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar

[2]Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar

[3]Associate Professor and HOD, Department of Pharmacology, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar

Received: 25-07-2024 / Revised: 23-08-2024 / Accepted: 26-09-2024

Corresponding Author: Dr. Jeetendra Kumar

Conflict of interest: Nil

Abstract:

Background: Fungal infections are a major concern for both patients and treating physician, especially those affecting skin. Dermatophytosis/tinea is one of the most common skin diseases affecting people across the world; caused by superficial fungus which invade and multiply within the keratinized tissue (skin, hair, nails). Approximately, 20-25% of the world population is affected by tinea. Aim of the present study was to compare the efficacy and safety of oral griseofulvin and oral terbinafine in tinea capitis among children aged 3–14 years.

Methods: This open-label, prospective, comparative study was conducted at Department of Pharmacology with collaboration of Pediatrics and Dermatology department of JLNMCH, Bhagalpur, Bihar from January 2023 to June 2023. Children between the ages of 3 and 14 years were enrolled for over 24 months. Patients with clinically diagnosed and laboratory-confirmed tinea capitis were randomized into two groups of 50 each. Group A was given oral griseofulvin for 8 weeks and Group B was given oral terbinafine for 4 weeks.

Results: Early response was obtained in Group B treated with terbinafine, and a statistically significant reduction in clinical symptoms was obtained at 4 weeks compared to griseofulvin with P = 0.044. Mycological cure was achieved at the end of 6 weeks in the terbinafine group, with P = 0.034 compared to the griseofulvin group in which 3 patients remained KOH positive at 8 weeks.

Conclusion: Both drugs were well tolerated with no serious adverse effects. Terbinafine is an effective alternative to griseofulvin in pediatric patients with tinea capitis with a shorter duration of treatment and fewer adverse effects.

Keywords: Griseofulvin; Terbinafine; Tinea Capitis; Pediatric Fungal Infection.

Introduction

Tinea capitis (T. capitis) is a dermatophytic infection of the scalp, and the associated hair loss. It is the most common pediatric dermatophytic infection worldwide. T capitis is becoming a public health problem due to its increasing incidence.

Major fungi causing dermatophytosis are Trichophyton, Microsporum, and Epidermophyton [1]. Recently, there is a change in the pattern of tinea seen as an increase in the occurrence of difficult to treat recalcitrant, recurrent, and chronic dermatophytosis [2]. Various factors such as global warming, hot and humid climate, migration of laborers, increased frequency of wearing tight and synthetic clothing, obesity, sedentary lifestyle, increasing prevalence of Trichophyton mentagrophytes and poor compliance of patients are reasons for the treatment resistant tinea [3,4]. Apart from this, another major factor contributing to this is the widespread abuse of topical steroid antifungal combination creams by the patients, mostly available as an Over The Counter (OTC) purchase or when prescribed by practitioners or quacks [5]. Terbinafine, the first line systemic drug for the treatment of dermatophytosis, acts by inhibiting the enzyme squalene epoxidase involved in the synthesis of ergosterol which is necessary for the formation of fungal cell membrane [6].

Griseofulvin is the medication of choice, and the treatment lasts between 4 and 8 weeks. Griseofulvin can cause an increase in the risk of hepatic side effects, hypersensitivity reactions, photosensitivity, hematologic effects, and severe skin reactions. Griseofulvin also requires longer treatment to produce its therapeutic effect. Due to these disad-

vantages, alternative treatment modalities are being considered. Alternative treatments include azole antifungal drugs such as itraconazole and fluconazole and allylamine antifungals like terbinafine. To lessen the inflammatory response and lower the likelihood of permanent alopecia, specific presentations like kerion require systemic steroids for a brief period of time. The oral antifungal medication is used in conjunction with this steroid therapy.[7]

Materials and Methods

This randomized, open-label, comparative study was conducted at Department of Pharmacology with collaboration of dermatology department, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar from January 2023 to June 2023 with children aged 3–14 years. Children clinically diagnosed, KOH microscopy (20% potassium hydroxide)-confirmed uncomplicated tinea capitis. Patients attending the outpatient department of dermatology were included in the study.

100 patients suffering from uncomplicated tinea capitis fulfilling the eligibility criteria were enrolled in the study after obtaining informed consent/ assent. The sample size was arrived at, assuming a 95% confidence interval and power of 80%, and assuming a dropout rate of 20%.

The following patients were included – (a) all new cases of uncomplicated tinea capitis clinically diagnosed by a dermatologist and KOH (20% potassium hydroxide) microscopy confirmed, (b) age group between 3 and 14 years attending the dermatology outpatient department, and (c) patient's parent/guardian who is willing to give informed written consent (assent) for the above study and regular follow-up.

Old cases who were taking antifungals for any disease in the past 8 weeks, persons allergic to either griseofulvin or terbinafine, children under treatment for other systemic illnesses, and history of liver and renal insufficiency were excluded from the current study.

100 patients fulfilling the eligibility criteria on the face were allocated into 2 study groups A and B-50 each. They were randomly assigned to one of the 2 treatment schedules using a computer-generated random number table. Instructions were given to the parent/guardian to give head wash with non-medicated shampoo (without antifungal) twice weekly. The dose of the medications received was Group A - griseofulvin 10–20 mg/kg/day at night with fatty food and Group B - terbinafine 62.5 mg/day, OD for children of 10–20 kg at night (1/4 tablet of 250 mg tab); 125 mg/day, OD for children of 20–40 kg at night (½ tablet of 250 mg tab); 250 mg/day, and OD for children of above 40 kg at night (1 tablet). The duration of treatment was 8 weeks for griseofulvin and 4 weeks for terbinafine.

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean ± SD, and results on categorical measurements are presented in numbers and percentages (%). Significance is assessed at a 5% level of significance.

The assumptions on data were made – dependent variables should be normally distributed. Normality was tested using the Shapiro–Wilk test in frequency statistics. The samples showing non-normal distribution were analyzed accordingly. The Chi-square or Fisher exact (if the value of the variable was <5 in any of the cells) test has been used to find the significance of the study.

Results

The summary of baseline demographic parameters and clinical parameters is depicted in Table 1.

Table 1: Summary of baseline demographic parameters and clinical parameters in between the two groups

Parameters	Category	Group A (n=50) n(%)	Group B (n=50) n(%)	P value
Age	<5 years	3 (6%)	2 (4%)	0.298*
	6–10 years	31 (62%)	22 (44%)	
	11–14years	16 (32%)	26 (52%)	
Gender	Male	31 (62%)	35 (70%)	0.481$
	Female	19 (38%)	15 (30%)	
Region	Urban	38 (76%)	36 (72%)	0.648$
	Rural	12 (24%)	14 (28%)	
Duration of tinea	<1 month	3 (6%)	3 (6%)	0.578*
	1–2 months	43 (86%)	46 (92%)	
	>2 months	4 (8%)	1 (2%)	

***Fisher's exact test, $Chi-square test, P-value of <0.05 is considered statistically significant**

There was no statistically significant difference noted between the two groups. Efficacy assessment was one at baseline, 2 weeks, 4 weeks, 6 weeks, and 8 weeks. The patients were clinically assessed on the basis of four main clinical features – erythema, scaling, edema, and itching. All patients had itching at the baseline, and only

3 patients in Group A had edema. The summary of the progression of clinical symptoms from baseline to 8 weeks through follow-ups at 2, 4, and 6 weeks is elucidated in Table 2.

Table 2: Clinical symptoms from baseline to 8 weeks through follow-ups at 2, 4, and 6 weeks

Clinical Symptoms	Group A				Group B			
	Erythema	Scaling	Edema	Itching	Erythema	Scaling	Edema	Itching
Baseline	28	48	3	50	43	48	0	50
2 weeks	19	44	0	38	17	35	0	27
4 weeks	6	26	0	15	2	2	0	4
6 weeks	0	0	6	0	0	0	0	0
8 weeks	0	0	0	3	0	0	0	0

All efficacy parameters were compared within the group using repeated measures ANOVA, and it signified that both drugs were efficacious. For between the group analyses, unpaired t-tests were performed. Statistically significant results were scaling at 4 weeks, and itching at 2 weeks was better overcome by terbinafine (P = 0.041 and P = 0.044, respectively), whereas griseofulvin required a longer duration. Microbiological efficacy was measured using KOH negativity rates. As depicted in Table 3, terbinafine showed better negativity rates at 4, 6, and 8 weeks.

Table 3: Measurement of microbiological/mycological efficacy using KOH negativity rates between the two groups

Visit	Number of patients with KOH negativity		P value[#]
	Group A (n=50)	Group B (n=50)	
2weeks	0	23	-
4weeks	9	45	0.038
6weeks	28	48	0.046
8weeks	47	50	0.032

#Unpaired t-test, P<0.05 was considered statistically significant

Safety assessment: adverse events were reported in both groups, the incidence of adverse drug reactions was high in the griseofulvin group (56%), and gastrointestinal side effects were more common (25%). The terbinafine group also had 11 adverse events (22%). All adverse events were mild and none warranted the discontinuation of therapy. All adverse events were reported to the adverse drug reaction monitoring center, and symptomatic treatment was provided.

Table 4 demonstrates the adverse event pattern between the two groups.

Table 4: Pattern of adverse drug reactions between the two groups

Adverse drug reactions	Group A (n=28)	Group B (n=11)
Nausea and vomiting	15	4
Diarrhea	10	2
Headache	3	5

Discussion

Systemic antifungal medication is necessary for treating tinea capitis. Although topical antifungal medications seldom produce side effects, they are not advised for the management of tinea capitis on their own since they do not reach the deep dermal roots of the hair follicles. However,topical antifungal medication can be utilized as an adjunctive treatment to systemic antifungals and can be used to lessen spore transmission. Combining oral and topical antifungal treatments may improve the cure rate.[8] In our current study, we compared two oral drugs, and both were efficacious clinically and mycological. Griseofulvin, which is considered the drug of choice for tinea capitis, and alternative terbinafine were compared. The best evidence shows that newer medications, including terbinafine, itraconazole, and fluconazole, may be equivalent to griseofulvin for children having tinea capitis induced by trichophyton species, according to the most comprehensive Cochrane review of the oral therapy for tinea capitis.[9] Even though they could be more expensive, newer medications might be favored since shorter treatment durations might enhance treatment adherence.

Terbinafine was shown to be favorable for trichophyton infestations of the scalp; however, griseofulvin was preferred for microsporum infections, according to a thorough systematic analysis that used more published data.[10] Tinea capitis is still a widespread illness, with prevalence rates in some areas surpassing 40%.[11,12] Even 50 years ago, however, there had been a public and political desire to discover effective control methods; now, this

infection is not seen as a health priority. Tinea capitis may be controlled, and the development of an immunizing antigen is theoretically feasible given the current knowledge of immunology and host vulnerability, including the most recent discoveries of particular CARD9 gene mutations linked to widespread deep dermatophytosis.[13] This strategy is still some time off; therefore, the best way to stop illness from spreading further is to strengthen surveillance in schools and treat cases as soon as they arise with antifungals.[14] Our study strengths were – randomized study design, usage of both microbiological and clinical parameters, multiple follow-up visits, and choice of appropriate control. Ourstudy had the following limitations – (A) In this study, the fungal culture could not be done due to a great number of false-negative results received in the pilot study, and other reasons included time constraints and cost; (B) no attempt was carried to identify the relapse rates in each of the groups. It could have been better if the rate of relapse in each of the groups if any was documented; (C) open-label study design; (D) as combination therapy is suggested, a combination of topical agents would have been more generalizable. In the future, studies should be conducted to compare griseofulvin and terbinafine with azoles using a blinded randomized study design. A combination of topical and systemic agents for the treatment of tinea capitis would be more practical as dermatologists usually prescribe that in clinical practice.

Conclusion

A statistically significant reduction in clinical features was observed at the end of 4 weeks in the terbinafine group, and mycological cure was achieved at the end of 6 weeks in the terbinafine group than with the griseofulvin group. Both the drugs were well tolerated with no serious adverse effects. Therefore, terbinafine is an effective alternative to griseofulvin in pediatric patients with tinea capitis with a shorter duration of treatment and fewer adverse effects.

References

1. Rajabian A, Hosseinzadeh H. Dermatological effects of nigella sativa and its constituent, thymoquinone. In: Preedy VR, Watson RR, editors. Nuts and Seeds in Health and Disease Prevention. San Diego, CA: Elsevier; 2020. Pp. 329–55.
2. Dogra S, Uprety S. The menace of chronic and recurrent dermatophytosis in India: Is the problem deeper than we perceive? Indian Dermatol Online J. 2016; 7(2):73-76.
3. Rengasamy M, Chellam J, Ganapati S. Systemic therapy of dermatophytosis: Practical and systematic approach. Clin Derm Rev. 2017; 1(3):19.
4. Babu PR, Pravin A, Deshmukh G, Dhoot D, Samant A, Kotak B. Efficacy and safety of terbinafine 500 mg once daily in patients with dermatophytosis. Indian J Dermatol. 2017; 62:395-99.
5. Dutta B, Rasul E, Boro B. Clinico-epidemiological study of tinea incognito with microbiological correlation. Indian J Dermatol Venereol Leprol. 2017; 83(3):326.
6. Lipner SR, Scher RK. Onychomycosis: Treatment and prevention of recurrence. J Am Acad Dermatol. 2019;80(4):853-67.
7. Al Aboud AM, Crane JS. Tinea capitis. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2022.
8. Leung AK, Hon KL, Leong KF, Barankin B, Lam JM. Tinea capitis: An updated review. Recent Pat Inflamm Allergy Drug Discov 2020; 14:58-68.
9. González U, Seaton T, Bergus G, Jacobsson J, Martínez- Monzón C. Systemic antifungal therapy for tinea capitis in children. Cochrane Database Syst Rev 2007; 17:CD004685.
10. Tey HL, Tan AS, Chan YC. Meta-analysis of randomized, controlled trials comparing griseofulvin and terbinafine in the treatment of tinea capitis. J Am AcadDermatol 2011; 64:663-70.
11. Alvarez MS, Silverberg NB. Tinea capitis: Current status. Cutis 2006; 78:189-96.
12. Patel GA, Schwartz RA. Tinea capitis: Still an unsolved problem? Mycoses 2011; 54:183-8.
13. Lanternier F, Pathan S, Vincent QB, Liu L, Cypowyj S, Prando C, et al. Deep dermatophytosis and inherited CARD9 deficiency. N Engl J Med 2013;369:1704-14.
14. Hay RJ. Tinea capitis: Current status. Mycopathologia 2017;182:87-93.