

Original article

Fluconazole pulse therapy: effect on inflammatory tinea capitis (kerion and agminate folliculitis)

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Abstract *Background* Tinea capitis, a fungal infection of scalp hair, can be caused by any species of either *Trichophyton* or *Microsporum* genera. It requires systemic antimycotic therapy. Griseofulvin is the only FDA approved drug for the treatment of this dermatophyte infection. Fluconazole pulse therapy is cost effective in tinea capitis.

Objective The study was aimed to assess the efficacy of fluconazole pulse therapy in patients with inflammatory (kerion and agminate folliculitis) tinea capitis and to study fluconazole as an alternative therapy to griseofulvin.

Patients and methods The open clinical trial was carried out in the outpatient department of “Baqai Institute Skin Diseases”, Baqai Medical University, Karachi and Ziauddin Medical University, Karachi, from 1st February, 2003 till 31st January, 2004 over a period of 1 year. Clinically suspected cases of tinea capitis, suffering from inflammatory lesions (kerion and agminate folliculitis), were included in the study. Specimens were taken from the affected scalp along with hair for light microscopy and subsequent inoculation onto Sabouraud’s media for fungal culture. All the mycologically confirmed patients fulfilling the inclusion criteria were given weekly oral pulses of fluconazole, 150mg for a period of 6 weeks. The patients were followed up weekly, during therapy and then fortnightly to look for clinical improvement as well as any side effects for a period of 16 weeks (10 weeks after completion of the therapy). The clinical signs (erythema, scaling, edema, pustules, pruritus and hair loss) were assessed on four-point scale graded from 0-3 (0= absent, 1= mild, 2= moderate, 3 = severe).

Results Of the 16 patients (kerion and agminate folliculitis) completing the study, there were 9 (56.3%) males and 7 (43.7%) females, the age range being 7-14 years. The clinical findings included erythema, scaling, edema, pustules, pruritus and hair loss. Fungal culture revealed *Microsporum canis* in all patients. Clinical improvement was apparent by the end of 3rd week of therapy. Regrowth of hair was evident by the end of 10th week and progressed slowly by the end of follow up period i.e. 16th week. Clinical cure rate was 69% and mycological cure rate 81.2% by the end of 6th week. At the end of 10th week, the clinical and mycological cure rates were 75% and 87.5%, respectively. At final evaluation, the relevant cure rates were 93.5% and 100%, respectively.

Conclusion Intermittent short duration therapy with fluconazole is effective for the inflammatory types (kerion and agminate folliculitis) of tinea capitis.

Key words

Tinea capitis, fluconazole, kerion, agminate folliculitis

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Introduction

Tinea capitis is a fungal infection characteristically affecting children between 4 and 14 years of age. Tinea capitis, a fungal infection of scalp hair, can be caused by any species of either *Trichophyton* or *Microsporum*.¹

Large family size, crowded living conditions, and low socioeconomic status may contribute to an increased incidence of tinea capitis. Transmission occurs via infected persons, shed infected hair, animal vectors, and fomites. Clinically it is characterized by erythema, scaling, pruritus and alopecia.⁵ Clinical patterns of the disease include inflammatory (kerion, favus and agminate folliculitis) and non-inflammatory (grey patch and black dot) types.¹

Tinea capitis, a common problem in our society demands an adequate antimycotic therapy.² Griseofulvin is the only FDA approved drug for the treatment of this dermatophyte infection.^{3,4} The new antimycotic agents e.g. terbinafine, itraconazole and fluconazole are effective in tinea capitis but are not cost effective being out of reach of most patients in Pakistan.⁵ Fluconazole, pulse therapy is cost effective in tinea capitis.⁴ Fluconazole, a triazole has broad spectrum antifungal activity, especially active against clinically important members of the three genera i.e. *Microsporum*, *Trichophyton* and *Epidermophyton*.⁶ Absorption after oral ingestion is fast, as the presence of food at gastric pH will not effect its absorption.⁷ The concentration of drug achieved in skin and its appendages is 50 times higher than that from plasma and its clearance from skin and hair is slower as well.⁷ Fluconazole works by inhibition of the fungal cytochrome P-450 dependent 14- α demethylase, the key enzyme in ergosterol synthesis.⁶

The study was aimed to see the efficacy of fluconazole pulse therapy in patients with inflammatory types (kerion and agminate folliculitis) of tinea capitis and to study fluconazole as an alternative therapy to griseofulvin.

Patients and methods

The open clinical trial was carried out in the outpatient department of "Baqai Institute Skin Diseases", Baqai Medical University, Karachi and Ziauddin Medical University, Karachi, from 1st February, 2003 till 31st January, 2004 over a period of 1 year. Clinically suspected cases of tinea capitis, suffering from inflammatory lesions (kerion and agminate folliculitis), were included in the study. After a detailed history and clinical examination, the lesional skin was examined under Wood's lamp to look for fluorescence. Specimens were taken from the affected scalp along with hair follicles for light microscopy after staining with 25% potassium hydroxide. The specimens obtained were then inoculated onto Sabouraud's media, containing chloramphenicol and cycloheximide for fungal culture. Colonial morphology and microscopy of teased amount of a mature colony stained with lactophenol cotton blue, confirmed the positive cultures.

Patients belonging to both sexes with a clinical as well as mycological evidence of tinea capitis were included in the study. Patients having any systemic or local antifungal therapy for past 2 months were excluded. Patients on any other concomitant therapy were also excluded. Patients weighing less than 20 kg were also ruled out from the study.

All the mycologically confirmed patients fulfilling the inclusion criteria were given weekly oral pulses of fluconazole, 150mg for a period of 6 weeks. The patients were followed up every week, during therapy and then fortnightly to look for clinical improvement as well as any side effects for a period of 16 weeks (10 weeks after the completion of therapy). The clinical signs (erythema, scaling, edema, pustules, pruritus and hair loss) were assessed on four point scale graded from 0-3 (0= absent, 1=

mild, 2= moderate, 3= severe). Other investigations included hematological and biochemical profile, urine examination and X-ray chest.

Results

Of the 16 patients (kerion and agminate folliculitis) completing the study, there were 9 (56.3%) males and 7 (43.7%) females, the age range being 7-14 years. The mean age of presentation was 9.4 years. Eight patients (50%) had a history of exposure to pet animals and 9 (56.3%) patients revealed green fluorescence on Wood's light examination. The clinical findings included erythema, scaling, edema, pustules, pruritus and hair loss. Fungal culture revealed *Microsporum canis* in all the patients as identified by the typical colonial morphology i.e. whitish hue on the upper surface and yellow pigment on the reverse side. Microscopy revealed spindle shaped macroconidia. The clinical improvement was apparent by the end of 3rd week of therapy. The improvement continued not only as the therapy proceeded but also during the follow up period. Regrowth of hair follicles was evident by the end of 10th week and progressed slowly by the end of follow up period i.e. 16th week. Clinical cure rate was 69% and mycological cure 81.2% by the end of 6th week. At the end of 10th week, the clinical and mycological cure rates were 75% and 87.5% respectively. At final evaluation, the relevant cure rates were 93.5% and 100% respectively.

Only 2 patients complained of mild GIT upset, and there were no complains of any systemic toxicity. Any changes in the biochemical profile were not seen. The therapy was well tolerated by all the patients.

Discussion

Tinea capitis is a common pediatric dermatological problem. Systemic antifungals are the mainstay of treatment in tinea capitis and topical medication may be ineffective.¹ Griseofulvin, the most cost effective drug is always the drug of 1st choice. It is the only FDA approved drug for the treatment of the dermatophyte infection of scalp.⁴ Griseofulvin due to its efficacy, cost effectiveness and less number of hazards is still used in many countries.⁸ The new antimycotic agents like terbinafine, itraconazole and fluconazole are effective in tinea capitis but are not cost effective and are out of reach of most patients in Pakistan.⁵ Fluconazole, as an alternative to griseofulvin is not specifically approved by FDA for the treatment of tinea capitis.⁶ However, it has been approved for the treatment of different types dermatophyte infections in children over 6 months of age. Various regimes of the drug have been used in the management of tinea capitis. Solomon *et al.*⁹ reported a cure rate of 89% in patients with tinea capitis at a dose of 6-mg/ kg body weight daily for 20 days. Another regimen used has been in a dose of 5-mg/ kg daily for a period of 4 weeks.¹⁰ Gupta *et al.*¹¹ treated 20 children suffering from tinea capitis with weekly pulses of fluconazole 8 mg/ kg for 4-6 weeks, with no relapses even 16 weeks after completion of the therapy. Further reports confirm that intermittent short duration therapy with fluconazole is effective for tinea capitis.¹² Side effects of fluconazole include GIT disturbances, deranged liver function tests, skin eruptions and bone marrow suppression,¹² thrombocytopenia, angioedema,¹³ anaphylaxis,¹⁴ and Stevens-Johnson syndrome¹⁵ are a few other rare side effects of fluconazole.

In the current study, the clinical and mycological cure rates were 93.5% and 100%, respectively. These findings are quite consistent with the past studies reported in literature.⁹⁻¹¹ The clinical improvement was assessed by observing the clinical parameters, showing gradual improvement with therapy. Hair loss improved slowly and was not complete in any of the patients at the end of the study. The regrowth of hair follicles requires a longer duration of time.

The treatment was well tolerated, with no serious adverse effects. Mild GIT upsets were the only complaints in 2 of the patients which however settled as the therapy progressed. Thus, the regimen appears to be effective, safe and is associated with high compliance.

Griseofulvin is effective against dermatophyte infections of skin, hair and nails.⁸ The most cost effective drug is always the drug of first choice in tinea capitis.⁸ It has good antimycotic and anti-inflammatory effects. However, griseofulvin requires daily dosage over a period of six weeks. It may lead to decreasing drug compliance and an increase in side effects.¹⁸ Another disadvantage may be the ingestion of this drug with fatty meals. Moreover, the pathogens are becoming less sensitive to ketoconazole, itraconazole and griseofulvin due to widespread use of these drugs.¹² Hussain *et al.*¹⁰ have already claimed that newer antifungals can be used as an alternative to griseofulvin. Having not been used exclusively, fluconazole is more effective than other antifungals in eradicating the implicated organisms in tinea capitis.¹² Fluconazole with an efficacy similar to that of griseofulvin with its antimycotic and anti-inflammatory effects is a useful drug for the management of tinea capitis. The presence of food at gastric pH doesn't affect its absorption.⁶ Fluconazole penetrates scalp hair, where it

remains for an extended period even after cessation of the therapy, thereby explaining the efficacy of intermittent dosage.¹⁶ The concentration of drug achieved in skin and its appendages is 50 times higher than that from plasma and its clearance from skin and hair is slower as well.³¹⁻³³ Fluconazole in weekly pulses may be preferred over griseofulvin for the treatment of tinea capitis for the convenience of dosage making it a cost-effective remedy.

Conclusion

Intermittent short duration therapy with fluconazole is effective and safe for the inflammatory types (kerion and agminate folliculitis) of tinea capitis. Further trials are required to confirm its efficacy in other types of tinea capitis i.e. favus, grey patch and black dot types.

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