Saudi Pharmaceutical Journal (2009) **17**, 243–248

King Saud University

Saudi Pharmaceutical Journal

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Safety and efficacy of terbinafine in a pediatric Iranian cohort of patients with Tinea capitis

Ali M. Sabzghabaee [a,*], Parwin Mansouri [b], Mahboobeh Mohammadi [b]

[a] *Isfahan Pharmaceutical Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran*
[b] *Tehran University of Medical Sciences, Tehran, Iran*

Received 10 February 2009; accepted 22 March 2009
Available online 7 August 2009

KEYWORDS

Terbinafine;
Tinea capitis;
Clinical trial

Abstract *Background and objectives:* Tinea capitis is a common infection of the scalp and hair shaft caused by dermatophyte fungi that mainly affects prepubescent children. Systemic therapy is required for treatment and to prevent spread. The aim of present study was to assess the effect of terbinafine for Tinea capitis treatment in children.

Methods: Thirty Iranian pediatric patients with a clinical diagnosis of Tinea capitis were enrolled in the study. The Study was conducted in a general and referral teaching hospital (Imam Medical Centre – Tehran, Iran) from 2006 to 2007. Eligible patients with less than 20 kg of body weight were given 62.5 mg terbinafine, and for patients between 20 and 40 kg the dose was 125 mg, on the first visit. All patients had the second clinical visit and second samples for microscopic study were taken. For each patient, direct mycology test (KOH test) and mycological culture were carried out before the study was started and after second, fourth, fifth, sixth and eighth weeks. Probable drug's adverse effects were also recorded.

Results: Based on the results of mycological culture of patients' lesions, *Microsporum canis* and *Trichophyton sheonlini* were considered as major causes of Tinea capitis in these children. Out of 30 study patients, KOH test of 93% in the 5th week and 100% in the 6th week was negative. All patients healed completely from signs of infection, after six weeks. Also, no severe side effects were seen in any patients.

Conclusion: According to the results of this study, the use of terbinafine is an effective therapy in Iranian cases of Tinea capitis in children without severe side effects.

* Corresponding author.
E-mail address: sabzghaba@pharm.mui.ac.ir (A.M. Sabzghabaee).

1319-0164 © 2009 King Saud University. All rights reserved. Peer-review under responsibility of King Saud University.
doi:10.1016/j.jsps.2009.08.003

Production and hosting by Elsevier

1. Introduction

Skin dryness can discourage colonization by microorganisms, and the shedding of epidermal cells may inhibit many microbes from permanent residence. Occlusion of the skin with nonporous materials can interfere with the skin's barrier function by increasing local temperature and hydration. When the protective mechanisms of the skin failed or be inhibited, cutaneous

infection may occur (Hainer, 2003). Dermatophytes require keratin for growth, so they are restricted to hair, nails, and superficial skin and these fungi do not infect mucosal surfaces. Dermatophytoses are referred to as "tinea" infections. They are also named for the body site involved.

Tinea capitis (ringworm) is widespread throughout the world, and above all in Africa, Asia, South-eastern Europe and even in UK it is one of the most frequent forms of dermatomycosis (Frieden and Howard, 1994). A community point prevalence study from London suggested a disease prevalence of about 2.5% with a carriage rate of between 12% and 47% among schoolchildren (Hay et al., 1996). The disease rarely affects mature patients (but in post-menopausal women) (Aste et al., 1966) and is mostly found in children almost irrespective of age or sex (Elewski, 1966). Scalp and hair shaft are the most common sites of infection. Transmission is fostered by poor hygiene and overcrowding, which may have a role in transmission of disease through contaminated hats, brushes, pillowcases, and other inanimate objects. After being shed, it should be noted that affected hairs can harbor viable organisms for more than one year after shedding (Hainer, 2003). Irregular or well-demarcated alopecia and scaling are common clinical features of ringworm. When swollen hairs fracture a few millimeters from the scalp, "black dot" alopecia is produced. Boggy, sterile, inflammatory scalp mass due to a cell-mediated immune response (kerion) and also occipital lymphadenopathy may be seen in Tinea scalp infection as well (Hainer, 2003). In some cases, patients have symptoms and clinical signs of minimal ringworm infection but they are still mycologically positive and presumed capable of transmitting infection.

Tinea capitis requires systemic treatment because generally, topical antifungals are unable to sufficiently penetrate the hair shaft to clear the infection and systemic therapy is usually indicated. Furthermore, the use of topical antifungal treatment alone may contribute to the creation of carriers (Fuller et al., 2003). The only licensed treatment is oral Griseofulvin, the most common approved drug for oral therapy. It is usually given at a dose of 10 mg/kg for 6–8 weeks and in resistant cases, longer treatment may be required at doses of up to 20–25 mg/kg (Elewski, 1966). Due to long time course of therapy, it is highly recommended to have a positive mycology result before starting (Ali et al., 2007) and in more complicated cases of this disease (patients with pustular Tinea capitis and kerion), use of antifungal creams or shampoos while waiting for the mycology results (to reduce the risk of progression) is indicated (Fuller et al., 2001). Regarding the prevalence of ringworm in pediatric patients, unfortunately the compliance with such a lengthy treatment regimen is poor and lack of a suitable pediatric formulation of griseofulvin (e.g. suspension) for this subpopulation in many countries including Iran makes the efficacy of griseofulvine therapy much more complicated. Furthermore, some patients do not respond to standard therapy and may require higher doses or prolonged durations. In a recent survey of griseofulvin treatment of Tinea capitis in a practice setting, approximately 40% of patients did not respond to the drug and required additional treatment (Abdel-Rahman et al., 1997). So, if an antifungal drug with sufficient efficacy on ringworm needs a shorter course of therapy and also has a more convenient dosage regimen with an acceptable safety, it could be considered as a real therapeutic rival for griseofulvin.

Terbinafine, which has an allylamine chemical structure, has been developed as a new class of ergosterol biosynthetic inhibitors that are functionally as well as chemically distinct from the other major classes of ergosterol-inhibiting antifungal agents (Ryder and Favre, 1997). The drug is highly effective against dermatophytes in vivo and in vitro (Ghannoum and Rice, 1999). In one review research, out of 21 studies with 1812 participants, the use of terbinafine for four weeks and griseofulvin for eight weeks showed similar efficacy in three studies involving 382 participants. So, newer treatments including terbinafine may be similar to griseofulvin in children with tinea capitis caused by Trichophyton species. Also, because of its fungicidal action, it requires shorter treatment period than griseofulvin (Gonzalez et al., 2007). Allylamines act by inhibiting early steps of ergosterol biosynthesis. This inhibition coincides with accumulation of the sterol precursor squalene and the absence of any other sterol intermediate, suggesting that allylamine inhibition of sterol synthesis occurs at the point of squalene epoxidation, a reaction catalyzed by squalene epoxidase (Ryder and Favre, 1997). Studies with isolated squalene epoxidase indicate that it is the target for allylamine activity (Ghannoum and Rice, 1999). Terbinafine has a considerable hepatic metabolism which may rise concern about the pharmacogenetic differences of drug metabolism in different populations and the safety of standard dosing regimen in genetically different populations (Ghannoum and Rice, 1999). The drug may also cause hepatotoxic effects on the liver which increases the above-mentioned concern (Wickersham, 2009).

Many studies have evaluated the efficacy of terbinafine in white Caucasian populations (some of them were sponsored by the manufacturer of the original brand product of the drug) (Fuller et al., 2001; Memisoglu et al., 1999; Haroon et al., 1996; Kullavanijaya et al., 1997; Caceres-Rios et al., 2000; Rademaker and Havill, 1998; Filho et al., 1998) but to knowledge of authors, there is not enough reliable data on both safety and efficacy of the drug in Iranian pediatric patients with ringworm. The aim of present study is to evaluate the safety and efficacy of terbinafine in a pediatric Iranian cohort of patients with Tinea capitis.

2. Methods

The study design was open label clinical trial which was conducted in a general and referral teaching hospital affiliated with Tehran University of Medical Sciences (Imam medical centre, Tehran, Iran) from 2006 to 2007. All pediatric patients (up to 12 years old) with clinical signs and symptoms of erythema, scaling, hair loss and scalp itching who were diagnosed for Tinea capitis by a registered dermatologist (PM) and by laboratory confirmation of primary diagnosis with a positive test of potassium hydroxide (KOH) were considered eligible for the study. During the study, patients with chronic or active liver disease or any undiagnosed rise of hepatic marker enzymes (e.g. ALT&AST), complicated gastrointestinal disease, concurrent seborrheic dermatitis, or other scalp conditions such as scabies, psoriasis, head lice, or atopic dermatitis or use of any oral/topical treatment for Tinea capitis in the past 2 weeks of therapy and also patients with signs and symptoms of hypersensitivity to terbinafine after the start of therapy were excluded. Sampling was random using convenient sampling