DOI: 10.2478/v10249-011-0002-3

Tinea capitis in Belgrade 1998-2002

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UDC 616.59-002.828

VERSITA

Abstract

Tinea capitis (TC) is a worldwide health problem and a specific therapeutic challenge. The objective of this study was to establish the causative agents and clinical types and to present management options for TC. From 1993 to 2002, we treated 354 children (61% were boys) with TC. The data for the period 1998-2002, were analyzed in detail. After clinical and Wood's light examination, specimens were directly microscopically analyzed and cultivated. Superficial TC was diagnozed in 230 (65%), and kerion in 124 patients (35%), respectively. Of 51 kerion patients, 3 children (6%) had erythema nodosum. Griseofulvin was given at a dose of 15 to 25 mg/kg (average: 18 mg/kg). A 100% cure rate was achieved. In the period 1998-2002, M. audouinii was predominantly found in superficial TC. Oral griseofulvin therapy should be accompanied by shaving the hair from the scalp and topical imidazole creams, which provides 100% cure rate of superficial TC (in 6.5 weeks) and of kerion (in 5.4 weeks).

Tinea capitis (TC) is a fungal infection of the scalp, hair follicles and the surrounding skin caused by dermatophytes, usually species in the genera *Microsporum* and *Trichophyton*. TC is predominantly an infection of children. The prevalence of tinea capitis remains low in developed countries, but on the contrary, it is endemic in many developing countries, especially in Africa, making it a significant infectious dermatological disease (1). *Microsporum canis* is the predominant pathogen worldwide, except in the United Kingdom and North America, where *Trichophyton tonsurans* is the most prevalent (2,3). Oral griseofulvin has been, and still is, the treatment of choice for most cases of tinea capitis (4, 5). This study assesses the freqency, causative species, clinical types and management of tinea capitis in Belgrade.

Subjects and methods

This retrospective study covered the period between 1993 and 2002. During this time, 354 children with TC were treated at the Pediatric Dermatology Unit of the Institute of Dermatovenereology, University Clinical Center, Belgrade. The authors of the study treated and followed-up the patients. The data for the period 1998-2002, were analyzed in detail.

The diagnosis was based on clinical signs and symptoms, Wood's light examination and mycological examinations. Hair stumps, skin scrapings and scales were taken using sterile scalpel blades. Each sample was subjected to direct microscopic examination using 30% potassium hydroxide solution, and cultivated on Sabouraud's dextrose agar, at 25 °C. Dermatophytes were detected by colony morphology and microscopic appearance. Wood's light examination was done on admission, during the treatment and at the end of treatment. Patients were divided into two clinical types: those with superficial TC, and those with kerion celsi.

Results

Of 354 patients, 215 (61%) were boys. The youngest patient was a 3-month-old infant, whereas the eldest patient was a 16-year-old girl. In all age groups, boys had a higher incidence of infection (boys : girls=1.6: 1). Majority of infected children were aged from 4 to 12 (71%) (Table 1).

Superficial TC was more frequent, found in 230 patients (65%), while kerion celsi was diagnozed in 124 children (35%).

The data for the period between 1998 and 2002 were analyzed in detail. In this period 176 children with TC were treated. Mycological cultures revealed the predominance of *Microsporum* species (81%). *M. audouinii* infection was found in 53% of patients, *M. canis* in 27%, *T. mentagrophytes var. granulare* in 13% and *T. rubrum* in 4%. Superficial TC was most frequently caused by Microsporum species, while kerion celsi was most frequently caused by *Trichophyton species*. Mycological cultures were positive in 122/176 (69%) patients with TC. Of these, mycological cultures were positive in 102/125 (82%) of patients with superficial TC, and only in 20/51 (39%) of kerion celsi patients. The correlation between the clinical types and isolated dermathophytes is shown in Table 2.

A very interesting change in the epidemiological profile was established in the period 1993-2002. While *M. canis* was the predominant pathogen between 1993 and 1997 (99%), in the period 1998-2002, *M. audouinii* became the first causative agent of TC: *M. audouinii* was found only in one patient in 1997, while in 2002 there were 14 cases of TC (Fig. 1).

Of 51 patients with kerion celsi, 3 patients (6%) had concomitant sings and symptoms of erythema nodosum. *T. mentagrophytes var. granulare* was isolated in all these patients.

Griseofulvin (microcrystalline) was the mainstay of therapy. Between 1998 and 2002, griseofulvin

Table 1. Tinea capitis in Belgrade, age and sex distribution (1993-2002)

	Number of patients			
Age (years)	Boys	Girls	Total	%
0-3.9	50	32	82	23.2%
4-7.9	96	67	163	46.0%
8-11.9	52	35	87	24.6%
12-15.9	17	5	22	14.4%
Total	215	139	354	100.0%

Table 2. Tinea capitis in Belgrade, clinico-etiologic correlations (1998-2002)

	Clinical variety			
Etiologic agent	**Superficial TC**	**Kerion celsi**	**Total**	**%**
M. audouinii	64	0	64	52.5%
M. canis	26	7	33	27.0%
M. persicolor	1	0	1	0.8%
M. gypseum	0	1	1	0.8%
T. mentagrophytes	6	10	16	13.1%
T. rubrum	3	2	5	4.1%
T. violaceum	1	0	1	0.8%
Trichophyton spp.	1	0	1	0.8%
Total	102	20	122	100.0%

was used in 162/176 (92%) patients. It was not used only in case of drug shortages, or some adverse effects (exanthema, urticaria). Terbinafine was used in 11 patients, itraconazole in 2, and ketoconazole in 1 patient. In all patients, topical antimycotics (imidazole creams, twice a day, after a thorough wash) were used together with systemic therapy. The infected area or the whole scalp was shaved (in disseminated /diffuse forms) at the beginning of treatment and 2-3 weeks later. With such a treatment a 100% cure rate was achieved. Patients were followed-up for clinical and mycological response. Patients were considered cured if the clinical presentation was unremarkable, Wood's light examination negative (in *Microsporum spp*.) and mycological cultures negative.

Griseofulvin was given at a dose of 15 to 25 mg/kg, the average dose was 18 mg/kg, but 77% of patients were treated with 15 to 20 mg/kg, while 23% of patients were treated with doses above 20 mg/kg. In patients with superficial TC, the average treatment duration was 6.5 weeks, and in kerion patients 5.4 weeks.

Apart from oral antimycotic therapy, patients with kerion, were concomitantly treated with oral antibiotics and some with oral corticosteroids. All patients with kerion received oral antibiotics (cephalexin or erythromycin). 10/51 (~20%) patients with kerion (the most severe cases) received prednisone, beginning with 0.5 to 1 mg/kg (an average dose of 0.85 mg/kg). The dose was gradually tapered and discontinued after 10 to 14 days (12 days on average).

Griseofulvin adverse efects were noted in 5/162 patients (3%). Elevation of transaminases was registered in 3 patients (1.9%), one patient (0.6%) developed urticaria and one patient (0.6%) presented with exanthematous rash. In patients with urticaria or exanthema, griseofulvin treatment was stopped, and another oral antimycotic was introduced. In children with abnormal liver function tests, transaminase levels were approximately twice the level. Following the advice of the pediatrician, the treatment was continued and patients were closely monitored. At the end of treatment, the levels showed spontaneous normalization.

Discussion

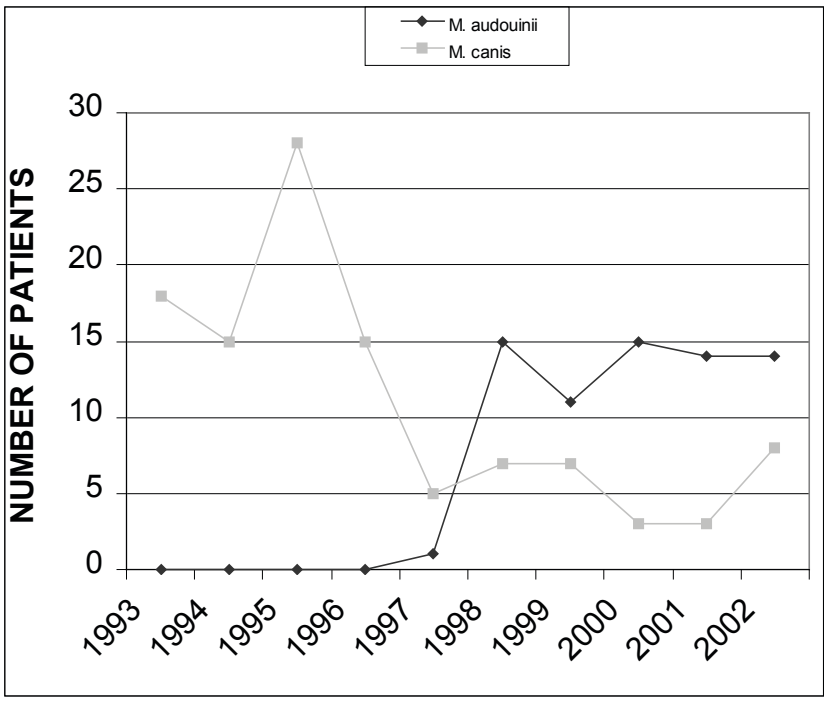

Figure 1. Tinea capitis caused by Microsporum spp.: epidemiology

The results of this study point to the high incidence of tinea capitis among examined children between 4 and 12 years, 70% of all cases being from this group. This observation is in accordance with other reports (6-8). The patients with TC were mostly from rural areas, surrounding Belgrade. The peak incidence was between 4 and 8 years of age; TC was twice as frequent among children between 4 and 8, than among younger (0-4 years old) and older (8-12 years old) children. There are at least two explanations: (a) children aged 0 to 4 are more attentively cared for, and (b) after the age of 12, sebum production is higher, reducing the risk of infection.

Boys were affected more frequently than girls; male domination was found in all our age groups (boys : girls = 1.6 : 1). Such a domination could have been caused by several reasons: (a) boys have shorter hair than girls, (b) sexual maturation and sebum production begin earlier in girls than in boys (c) generally, boys spend more time outside than girls, and they are at higher risk for getting an infection.

During the 1960s, in our country, mycotic infections of the scalp were most frequently caused by *Trichophyton spp*. The first cases of infection caused by *Microsporum* canis were diagnozed after transmission of this species by people working in Austria or Germany (9). During the last 10-year period, the majority of infections were caused by *Microsporum species* - 81%, while *M. audouinii* infection was present in 53%. Changes in the epidemiologic profile of TC infection is also found in other countries: in the USA, for example, M. audouinii was the primary causative agent of TC up to the 1950s, when increased Hispanic immigration introduced *Trichophyton tonsurans* to the USA (5). Today, *M. canis* is the predominant pathogen worldwide, except in the United Kingdom and North America, where *Trichophyton tonsurans* is prevalent (2,3). In countries close to Serbia and Montenegro, like Greece and Bosnia and Herzegovina, the infection is predominantly caused by *M. canis* (2,10). The epidemiologic profile of TC and its causative agents is not static, and a change was recently noted: *M. canis* was predominant up to 1997, and afterwards *M. audouinii* took the first position.

Although in our opinion erythema nodosum induced by kerion celsi of the scalp is not so exceptional, a detailed review of international literature surprisingly shows only nine published cases (11-16). Of these, *T. mentagrophytes* was identified in 7/9 cases, *T. gypseum* and *T. sulphureum* were isolated in two other patients (11-16). In our series, of 51 patients with kerion, there were 3 cases (6%) of erythema nodosum. *T. mentagrophytes var. granulare* was isolated in all these patients. Although *T. mentagrophytes* is not the most common etiological agent for kerion or superficial TC, it was detected in all patients with kerion associated with erythema nodosum. During treatment of kerion, erythema nodosum gradually disappeared.

Griseofulvin is a fungistatic agent that inhibits nucleic acid synthesis which arrests cell division at metaphase and impairs fungal cell wall synthesis. It demonstrates less drug interactions, than other antimycotic agents. Its advantages are that it is: licensed, inexpensive, syrup formulation, while prolonged treatment course is its main disadvantage. Griseofulvin was introduced in 1958 (17) and it represents the only agent approved by the U.S. Food and Drug Administration (FDA) for the treatment of tinea capitis in children (4). Our results show that all patients treated with griseofulvin, which was used in 162 patients, at a dosage of 15 to 25 mg/kg (18 mg/kg on average), during 4 to 8 weeks were cured. This observation is in accordance with other reports (4, 5, 6). In a study about dermatophytes and their in vitro antifungal sensitivity, griseofulvin proved to be the best drug with a sensitivity of 94.4% of isolates, followed by miconazole (a sensitivity of 75% of isolates) (18).

Many studies compared effects of griseofulvin (6-8 weeks) and terbinafine (3-4 weeks) in the treatment of TC. These studies showed that: (a) in case of *Trichophyton* infection the results were at least the same, comparing griseofulvin and terbinafine, (b) in case of *Microsporum* infection, the results were worse in patients receiving terbinafine (19,20). Today, terbinafine is the drug of second choice in the treatment of tinea capitis (4), but the drug of first choice in onychomycosis treatment (17,21). Recent studies on TC showed that the cure rate of 2% ketoconazole shampoo, as a monotherapeutic agent, was 33% (22). It is possible that the combination of 2% ketoconazole shampoo with oral griseofulvin,

might decrease the treatment time for TC (5).

In our opinion, based on experience including 354 TC patients during the last ten years, and on international literature, griseofulvin is definitely the first choice drug for treatment of TC in children, especially in patients with *Microsporum* infection which is found in 81% of patients in our country. Our experience and published literature data show that the dose of microcrystalline griseofulvin necessary to cure children with TC, is 15 to 25 mg/kg, not 10 mg/kg, recommended by British National Formulary (BNF) and some other books.

Some studies show that the efficacy of griseofulvin in the treatment of TC during 12 weeks was 88%, but without mentioning concomitant topical antimycotic treatment (23). In our study, systemic antimycotic therapy was always given with topical antimycotics, after shaving of the scalp, and the cure rate was 100%, in 6.5 weeks (on average) for superficial TC, and in 5.4 weeks in patients with kerion. Generally, the importance of topical adjunctive measures in the treatment of TC is not adequately emphasized in the literature. We consider that shaving of the affected areas, of the scalp, if the affection is disseminated/ diffuse, together with topical application of imidazole creams twice a day, are useful measures that reduce the treatment time.

Of 51 patients with kerion celsi, 10 children (~20%) were treated with griseofulvin and oral prednisone. In our series, prednisone was given at 0.5 to 1 mg/kg. The dose was gradually reduced and discontinued 10 to 14 days later (12 days on average). One study has shown that combination of oral prednisolone and griseofulvin does not result in additional objective or subjective improvement, compared to griseofulvin alone, in cases with kerion celsi (24). Our results showed that patients were cured without oral corticosteroids, but the period of inflammation was shorter in patients with prednisone, than in patients without it.

Tinea capitis is still a significant health problem in developing countries. However, the epidemiological profile in Serbia is changing now. *M. audouinii* is the predominant causative agent and similar change might take place in the surrounding countries as well as in other parts of Europe. Griseofulvin is a very effective therapy and we sugest that the treatment should be accompanied by local measures including shaving the scalp and use of topical imidazole creams. Such a combination offers a 100% cure rate of superficial TC in 6.5 weeks and in 5.4 weeks in patients with kerion.

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Tinea capitis u Beogradu 1998-2002. godine

Sažetak

Tinea capitis (TC) predstavlja zdravstveni problem koji se sreće u celom svetu i koji nameće specifične terapijske izazove.

Ciljevi: Ustanoviti učestalost, uzročne agense, kliničke tipove TC i predstaviti terapiju TC.

Metode: Od 1993. do 2002. godine, lečili smo 354 dece sa TC. Podaci za period 1998-2002. godine detaljno su analizirani. Pacijenti su pregledani klinički i pod Woodovom lampom, a uzorci mikroskopski i kultivisani na Sabouraudovom agaru.

Rezultati: 215 pacijenata (61%) bili su dečaci. Odnos dečaci : devojčice bio je 1,6 : 1. 71% pacijenata bilo je u uzrastu 4 do 12 godina. Superficijalna TC je dijagnostikovana kod 230 (65%), dok je kerion celsi dijagnostikovan kod 124 pacijenta (35%). U periodu 1993-2002. godine dominirali su uzročnici iz roda *Microsporum* (81%). U periodu 1993-1997. godine, *M. canis* je bio predominantni uzročnik, dok je od 1998. do 2002. godine predominantan *M. audouinii*. Od 51 deteta sa dijagnozom kerion celsi, 3 pacijenta (6%) imala su erythema nodosum i kod sva tri je izolovan *T. mentagrophytes var. granulare*. Grizeofulvin je bio osnovni lek i primenjivan je u dozi od 15 do 25 mg/kg tt (prosečno 18 mg/kg tt). Postizali smo izlečenje kod 100% pacijenata. Kod 10/51 dece sa kerionom, primenjivan je i prednizon per os, zajedno sa antimikotikom.

Zaključak: U periodu 1998-2002. godine *M. audouinii* je bio predominantan izazivač superficijalne TC. Sugerišemo da peroralna antimikotska terapija treba da bude praćena brijanjem kapilicijuma i topikalnom terapijom imidazolima, što omogućava izlečenje 100% pacijenata: superficijalne TC u proseku za 6,5 nedelja, a keriona u proseku za 5,4 nedelja.