Dermatophytosis: The Management of Fungal Infections

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Dermatophytosis is an infection of the hair, skin, or nails caused by a dermatophyte, which is most commonly of the Trichophyton *genus and less commonly of the* Microsporum *or* Epidermophyton *genera. Tinea capitis, tinea pedis, and onychomycosis are common dermatologic diseases that may result from such an infection. The treatment of fungal infections caused by a dermatophyte has been successful when treated with oral or topical antifungal agents. Terbinafine, itraconazole, and fluconazole are oral antimycotics that are effective in the treatment of superficial mycoses, although, depending on the severity of the infection, a topical antifungal may be sufficient.*

Dermatophytosis is an infection of the hair, skin, or nails caused by a dermatophyte, mostly frequently involving the genera *Trichophyton*, *Microsporum*, and *Epidermophyton*. Common dermatologic diseases that may result from such an infection include tinea capitis, tinea pedis, and onychomycosis. These diseases can be successfully treated with oral or topical antifungal agents depending on the severity and nature of the infection.

The mainstay treatment of fungal infections was griseofulvin, an oral antifungal agent, [1] having first been used in the late 1950s. [1] Ketoconazole, introduced in 1981, was one of the first broad-spectrum oral imidazoles. [2] Currently, this agent is infrequently prescribed in the United States to treat superficial fungal infections other than pityriasis versicolor because of the potential for hepatotoxicity. The triazoles, fluconazole and itraconazole, and the allylamine, terbinafine, are antifungal agents with a broad spectrum of activity against dermatophytes, nondermatophytes, and yeast. These antimycotics have an improved efficacy, a safer adverse event profile, and increased patient compliance as compared with the older agents, griseofulvin and ketoconazole. Furthermore, fluconazole, itraconazole, and terbinafine remain active in the skin, hair, and nails for a period after the cessation of the therapy. This article will discuss the treatment of tinea capitis, tinea pedis, and onychomycosis.

Tinea Capitis

Tinea capitis is a common fungal infection of the scalp, especially among prepubescent children, which has been increasing in incidence. Thirty years ago, *Microsporum audouinii* was a frequent cause of tinea capitis within North America, however, *Trichophyton tonsurans* has been the more recent frequent cause of this disease. [3, 4] The treatment of tinea capitis depends partly on the infecting fungal organism (*Microsporum vs. Trichophyton* tinea capitis) and may include treating individuals who are asymptomatic carriers.

Management

Treatment of tinea capitis requires an oral antifungal agent (Table I). Griseofulvin is the only Food and Drug Administration-approved drug for the treatment of tinea capitis; it continues to provide good efficacy, [6–11] although reports indicate that dosage regimens are higher and longer than in the past. [12] Griseofulvin is a fungistatic agent. It is quickly eliminated from the body and must be given continuously for a relatively long period, which may contribute to reduced patient compliance and decreased efficacy. In many countries, griseofulvin is available in an oral suspension, which can be advantageous when treating young children who are unable to swallow capsules or tablets.

Itraconazole and fluconazole, although not approved by the US Food and Drug Administration, have been used effectively to treat tinea capitis. Compared with griseofulvin, the dosing regimens required for the azoles are generally shorter, which may increase patient compliance and decrease the cost of the antifungal therapy. Continuous dosing with itraconazole for a period of 2–4 weeks has been successful in the treatment of tinea capitis. [9, 13, 14] A pulse-dosing schedule of itraconazole may also be feasible to reduce the amount of drug exposure, due to the long-term retention in tissues, thereby decreasing the cost of the therapy and the potential for adverse events. Pulse dosing has been studied using both itraconazole capsules (5 mg/kg/d; one pulse=1 week of therapy followed by 3 weeks without medication) and oral solution (3–5 mg/kg/d; 1 week on, 2 weeks off). [15–19] Further research is needed to determine whether pulse dosing of itraconazole should replace standard continuous dosing. In addition, research is needed to determine whether daily or weekly dosing is optimal for fluconazole. [20] Both drugs have a good safety profile in tinea capitis treatment, with most adverse events being mild and transient. [13, 20] Like griseofulvin, oral suspensions of both itraconazole and fluconazole are available. The former has been associated with a higher incidence of mild, transient gastrointestinal adverse events as compared with its capsule formulation.

Terbinafine, an allylamine agent, has been approved for use in tinea capitis in many countries worldwide. This agent has excellent absorption and remains in keratin for a period beyond the end of active dosing. [21] Effective treatment regimens for *T. tonsurans* tinea capitis are of a 2–4 week-duration, which is shorter than those required by griseofulvin. This approach may provide better compliance and a reduced cost of treatment. The efficacy of terbinafine in the treatment of tinea capitis is high, however, even higher efficacy or a shorter duration of therapy may be possible according to recent pharmacokinetic studies. [6, 10, 22, 23] It has been suggested that the optimal terbinafine dosages may need to be increased and administered on a mg/kg basis (>4.5 mg/kg/d, regardless of the treatment duration, both when *Trichophyton* and *Microsporum* species are the causative organisms) rather than the current standard terbinafine dosing regimen, which is <20 kg weight, 125 mg/d; 20–40 kg; 125–250 mg/d; and >40 kg, 250 mg/d. [6, 10, 22, 23] Further studies are needed to determine whether higher dosing will provide a more optimal efficacy than the current dosing regimen. Unlike griseofulvin and the azoles, no oral formulation is available for children who are unable to swallow tablets, however, to improve compliance, terbinafine can be powdered and added to food. [24] Most adverse events experienced with terbinafine are mild and transient. [25]

People in contact with infected individuals (e.g., people in the same household) should be cultured and assessed as potential asymptomatic carriers of the infection. Asymptomatic

carriers may need to be treated to prevent the spread of the fungal infection, particularly in cases of *Trichophyton* infection. [26–29] Topical therapy with antifungal shampoos such as selenium sulphide or povidone iodine shampoo may be sufficient to eliminate asymptomatic carriage of infection; however, in some instances, oral antifungal therapy may be necessary. [27] It is also important to discard or disinfect with bleach objects that may support fungal conidia, such as combs, hats, pillow, blankets, and scissors. This measure will help prevent subsequent infection or reinfection due to the transmission of conidia to the scalp. [28] Recent reports suggest that keeping children from school is not necessary, particularly children in higher grade levels, [30, 31] although the use of caps may help to reduce the spread of the contagion.

Tinea Pedis

Tinea pedis (athlete's foot) is a superficial skin infection of the feet and toes caused predominantly by dermatophytes. It is one of the most common forms of dermatophytosis. [47] There are three clinical presentations of tinea pedis: interdigital, moccasin, and vesicobullous. Interdigital tinea pedis is the most common form, characterized with fissuring, scaling, and maceration of the interdigital areas, particularly the 4/5-toe web. *Trichophyton rubrum* and *T. mentagrophytes* are the most common causative agents of infection. [33] "Dermatophytosis simplex" describes the most uncomplicated form of interdigital tinea pedis. Because of the already existing breakdown of the skin barrier by the dermatophytes, secondary bacterial infections are common. An overgrowth of bacteria can lead to highly inflamed, macerated skin, which is termed "dermatophytosis complex." [34]

Moccasin-type tinea pedis is characterized by fine silvery scales with underlying pink to red skin; it affects the soles, heels, and sides of the feet and is caused predominantly by *T. rubrum*. [35] It is characterized by dry, hyperkeratotic skin, which is relatively mild but, at the same time, is unattractive. More moderate to severe forms of moccasin have cracked and inflamed skin, with erythema and odor, and may include nail infections.

Vesicobullous tinea pedis is the least common form of tinea pedis; however, it is the most severe in characteristics with periods of acute and highly inflammatory vesicular or bullous lesions. [34] *T. mentagrophytes* is the most common causal organism. [35] Initial inflammation at the in-step of the foot may spread over the entire sole. [33] The mildest form involves the development of small, isolated vesicles filled with clear fluid, which may suddenly rupture independently and spontaneously resolve itself. Severe forms result in the coalescence of vesicles into large, acute, pruritic, spreading, ulcerative, and subsequently erosive bullae. [33–35]

Management

The severity of a tinea pedis infection will, to some degree, determine the course of treatment required. Mild infections may resolve using a topical agent; more severe presentations may require a treatment that can eliminate bacteria as well as fungus. Some topical therapies can provide both antifungal and antibacterial action. If inflammation is present, a treatment with a known anti-inflammatory action may be more optimal.

Some of the most common and efficacious treatments include the triazoles (i.e., fluconazole and itraconazole) and terbinafine. [2, 36–40] Due to the persistence of these agents in the keratinized layers of the soles and palms, short treatment periods are a viable option (

Table I). Oral antifungal agents provide an advantage in the treatment of tinea pedis as they are better able to penetrate the tissues, thereby resulting in a high efficacy [38]; however, with the use of oral agents there is a greater potential for adverse events and drug interactions as compared with topical antifungals. Therefore, the decision to use topical vs. oral antifungal therapy depends on factors such as the severity of the infection, previous response to topical antifungals, health status of the patient, the number/type of oral medications that the patient is taking, physician and patient preferences, and the patient's ability to afford the treatment.

Recurrence is very common among tinea pedis infections, many of which are chronic. It is important to understand how to control flare-ups and to prevent the spread of infection. Infected individuals should try to wear nonocclusive footwear, such as sandals, as often as possible; if this option is not a possibility, shoes should be alternated every 2–3 days. [1] Natural fiber socks and shoes should be worn and changed often. Communal areas, such as bathrooms, showers, and swimming pool floors, should be avoided since these are areas where infections spread easily. After showering, it is especially important that the feet are dried thoroughly, particularly between the toes, to eliminate moisture.

Onychomycosis

Onychomycosis is a common nail infection that is increasing in prevalence. Approximately 90% of reported cases of onychomycosis are due to dermatophytes, in particular *T. rubrum* and *T. mentagrophytes*, [41] with other potential pathogens including nondermatophyte molds and yeast (i.e., *Candida* species). Predisposing factors include tinea pedis, a positive family history of onychomycosis, increasing age, the male gender, trauma to the nail, diabetes, immunosuppression (e.g., human immunodeficiency virus-positive), poor peripheral (arterial) circulation, smoking, and possibly psoriasis. [42–47]

Management

The treatment of onychomycosis has improved greatly with the introduction of terbinafine, itraconazole, and fluconazole (Table II), as well as the nail lacquers ciclopirox and amorolfine. Some studies have shown that terbinafine may be the antifungal agent of choice when treating onychomycosis. For instance, the Lamisil itraconazole onychomycosis (LION) study, [48] a 72-week study comparing oral therapies of continuous terbinafine with intermittent itraconazole in the treatment of toenail onychomycosis caused by dermatophytes, demonstrated significantly superior efficacy parameters (mycologic cure, clinical response, clinical cure, and complete cure) of terbinafine. The Finnish and Icelandic participants of this study were followed up for 4 and 5 years, respectively. [49, 50] These studies demonstrated terbinafine as the superior treatment, with significantly fewer patients treated with terbinafine experiencing a mycologic or clinical relapse as compared with itraconazole-treated patients ($p < 0.01$). [49] Havu et al. [51] evaluated the long-term efficacy results of terbinafine as compared with fluconazole in the treatment of toenail onychomycosis. At Week 60, terbinafine was significantly better than fluconazole in achieving both a mycologic cure ($p < 0.001$) and a clinical cure ($p < 0.0001$).

Ciclopirox 8% and amorolfine 5% nail lacquers are topical antifungal agents that have a broad spectrum of action. These agents have been effective in the treatment of onychomycosis, although the latter is not approved in the United States for this indication. Some individuals prefer topical antifungals due to the potential adverse events with oral agents. Mild-to-moderate cases of onychomycosis, with no onycholysis or lunula

involvement, or superficial white onychomycosis, may be successfully treated with topical nail lacquers.

Oral and topical antifungal agents may also be used in a combination approach, although no such regimens are currently approved in the United States. [52–54]

Patients should be educated on proper nail care to help prevent relapse or reinfection of onychomycosis after a successful treatment. [55, 56] Nails should be kept cut short and clean. Similar to the prevention of tinea pedis, it is important to wear proper footwear when walking in communal areas (e.g., public bathrooms, gymnasiums, health spas), and feet should be dried completely following a bath or shower. Socks worn should be made out of absorbent material, such as cotton. Prophylactic treatment with topical agents may help prevent a reinfection or relapse of onychomycosis. [44]

Conclusions

The more recently available antimycotics for the treatment of dermatophytosis (fluconazole, itraconazole, and terbinafine) are not only efficacious but also have low systemic adverse events and short treatment durations, resulting in increased patient compliance.

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