

General Practice Update – Management of Fungal Skin and Nail Infections

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Causal Agents, Clinical Presentations and Management of Fungal Skin and Nail Infections

Speaker: Dr. D. Roberts

Superficial fungal infections are caused by dermatophytes plus candida and pityrosporum yeasts. Dermatophytosis is usually classified clinically according to the site of involvement: tinea capitis (scalp), T. corporis (body), T. cruris (groin), T. pedis (feet) and T. unguium (nails). One-half of all the cases of T. capitis and T. corporis are caused by zoophilic fungi, the rest due to anthropophilic fungi.

Tinea capitis

The clinical presentation of scalp infection includes a dry scaling patch of alopecia, a boggy swelling known as a kerion, or a generalized scaling with a minor degree of alopecia. *Microsporum canis*, *Microsporum audouinii*, *Trichophyton verrucosum* and *Trichophyton tonsurans* are the most frequent causes of tinea capitis. Other causes of alopecia, for example psoriasis, alopecia areata, discoid lupus erythematosus, sarcoidosis, bacterial infection and syphilis, should be excluded before a diagnosis of fungal infection is made.

Compared with griseofulvin, terbinafine has a higher overall efficacy (mycological plus clinical cure). A four-week course of oral terbinafine has a cure rate of 93% at week 12, compared to a cure rate of 80% with an eight-week course of oral griseofulvin.

Tinea corporis

All the above organisms that can cause tinea capitis can also affect glabrous skin. In addition, *Trichophyton rubrum* is also an important cause of tinea corporis. The differential diagnosis of tinea corporis includes granuloma annulare, discoid eczema, psoriasis and pityriasis rosea.

Tinea cruris

Tinea cruris occurs mainly in male. The differential diagnosis includes flexural psoriasis, erythrasma and infected eczema.

Tinea pedis

Toe-cleft maceration, especially when present in the fourth toe-cleft, almost always signifies a fungal infection. Acute toe-cleft infection is usually caused by *Trichophyton mentagrophytes*, and the moccasin type of tinea pedis is usually caused by *Trichophyton rubrum*. If maceration of toe-cleft is prominent, secondary bacterial infection has to be considered. Differential diagnosis of tinea pedis includes pustular and other forms of psoriasis, contact dermatitis, juvenile plantar dermatosis and Reiter's disease.

Tinea unguium

Only about half of all the cases of nail dystrophy are due to fungal infection. Other causes of nail dystrophy include psoriasis, lichen planus and peripheral vascular disease. Over 90% of all fungal nail infections are caused by dermatophytes, with *Trichophyton rubrum* responsible in about 90% of the cases. Superficial white onychomycosis can be found in AIDS patients and is usually caused by *Trichophyton mentagrophytes*.

Onychomycosis should be treated for the following reasons: (1) untreated onychomycosis will lead to an

increase in prevalence as a result of contamination of public places, (2) the condition does not resolve on its own, and (3) it predisposes the individual to secondary infection or complication, especially in diabetics, which may lead to amputation.

It is more important to have laboratory confirmation of the diagnosis of fungal nail infection than in other forms of fungal infection because the treatment duration is lengthy and systemic treatment would be needed. If therapeutic trial is started without mycological confirmation, it takes at least one year for any results to be observable.

Safety of oral antifungal agents

A post-marketing survey on the safety of oral terbinafine had been done involving 25,884 patients in Europe. The median duration of treatment was 12 weeks. The incidence of adverse events was 10.5%, which were usually mild and transient. The majority involved the gastrointestinal system (4.9%) or skin (2.3%). Terbinafine was considered a possible cause of 11 (0.04%) serious adverse events. These included two cases of serious skin reactions, one large bowel obstruction, one duodenal ulceration, one serious hepatobiliary dysfunction, one bronchospasm, one neutropenia, two cases of thrombocytopenia, one urticaria/angioedema and one leg oedema.

Among a cohort of 69,830 patients in the United Kingdom who had at least one prescription of an oral antifungal, there were 16 cases of acute liver injury. Acute liver injury was said to occur when one or more of the liver function parameters (aspartate-amino transferase, alanine-aminotransferase, alkaline phosphatase, total bilirubin) was two times higher than normal. Basing on patient-months, the relative risks of acute liver injury for the oral antifungal agents were as follows: fluconazole: 0.0, griseofulvin: 0.0, itraconazole: 17.7, ketoconazole: 228.0, terbinafine: 4.2.

Update on Oral and Topical Antifungal Treatment

Speaker: Prof. G. Evans

Diagnosis

It is important to have a correct diagnosis of fungal infection before starting treatment. In many instances,

treatment failure is due to a wrong diagnosis. For superficial mycoses, appropriate specimen should be collected for microscopy using potassium hydroxide, and culture using Sabouraud's agar. Nail clippings and subungal debris should be collected in cases of suspected fungal nail infection, and plucked hairs and skin scrapings of the scalp in cases of scalp infection. Culture failure is often due to poor specimen collection. It is important to get specimen as proximal as possible for laboratory diagnosis of fungal nail infection.

It is quite normal to get a few yeast colonies from non-sterile sites. In cases where cultures grow both dermatophytes and yeasts, the non-dermatophytes are probably secondary invaders of damaged nails rather than signifying a mixed infection. When the dermatophyte infection is treated, the yeast will go away. *Scytilidium* is the only mould that can invade nail and skin.

Efficacy of antifungal agents

When looking at the efficacy of a drug, the mode of action, the *in vitro* activity (minimal inhibitory concentration), the spectrum of activity and the kinetics should all be considered. All the new antifungal agents have good kinetic profiles. Azoles and allylamines inhibit the biosynthesis of ergosterol, which is essential to the integrity and overall development of the fungal cell membrane. Terbinafine, in addition, also inhibits the conversion of squalene to squalene epoxide, leading to a fungicidal accumulation of squalene.

Topical antifungal agents

Topical terbinafine, used once or twice a day, for one or two weeks, can achieve a cure rate of over 80% for tinea pedis, tinea cruris and tinea corporis. Compared with other topical antifungals in the treatment of tinea pedis, a one-week course of topical terbinafine was shown to be significantly better than four weeks' of topical clotrimazole, and was as good as four weeks' of topical miconazole. The shorter treatment duration with topical terbinafine may also improve compliance. The different formulations of terbinafine (cream, solution, gel) with equal concentration have the same efficacy. Topical treatment of onychomycosis, on their own, is not usually effective. A study demonstrated that the use of 5% amorolfine nail lacquer for six months in the treatment of distal onychomycosis resulted in a mycological cure of about 50%.

Oral treatment of onychomycosis

Terbinafine, at a daily oral dose of 250 mg for three months for the treatment of onychomycosis, has a cure rate of 75-80%, whereas itraconazole has a cure rate of 40-80%, when given at 400 mg per day for one week each month, for three to four months. Fluconazole has a cure rate of 50-70%, when given at 150 mg per day for one week each month. Some of the patients from the L.I.O.N. study had been entered into a long term follow up study (the Icelandic extension study). According to the speaker, this study confirmed that terbinafine is superior to itraconazole not only in terms of original cure rates over 72 weeks but also in having lower relapse rates over a further period of up to four years. The relapse rates in previously mycologically cured patients were 18% and 19% for the three- and four-month terbinafine groups as compared with 71% and 73% for the three and four pulses itraconazole groups.

Even for confirmed cases of onychomycosis, treatment failure still occurs in about 20% despite the use of terbinafine. The possible reasons include lack of compliance, poor absorption, no nail growth, immunosuppression, drug kinetic problems associated with a dermatophytoma, "mixed" infection, antifungal resistance, and resistant forms of fungus.

Learning points:

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