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A Study of Dermatophytic Infections in Geriatric Population

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ABSTRACT: Dermatophytes are fungi that require keratin for growth. These fungi can cause superficial infections of the skin, hair, and nails. Dermatophytes are spread by direct contact from other people (anthropophilic organisms), animals (zoophilic organisms), and soil (geophilic organisms), as well as indirectly from fomites. Dermatophyte infections can be readily diagnosed based on the history, physical examination, and potassium hydroxide (KOH) microscopy. Diagnosis occasionally requires Wood's lamp examination and fungal culture or histologic examination. Topical therapy is used for most dermatophyte infections. Cure rates are higher and treatment courses are shorter with topical fungicidal allylamines than with fungistatic azoles. Oral therapy is preferred for tinea capitis, tinea barbae, and onychomycosis. Orally administered griseofulvin remains the standard treatment for tinea capitis. Topical treatment of onychomycosis with ciclopirox nail lacquer has a low cure rate. For onychomycosis, “pulse” oral therapy with the newer imidazoles (itraconazole or flucona-zole) or allylamines (terbinafine) is considerably less expensive than continuous treatment but has a somewhat lower mycologic cure rate. The diagnosis of onychomycosis should be confirmed by KOH microscopy, culture, or histologic examination before therapy is initiated, because of the expense, duration, and potential adverse effects of treatment.

The dryness of the skin's outer layer discourages colonization by microorganisms, and the shedding of epidermal cells keeps many microbes from establishing residence.[1] However, the skin's mechanisms of protection may fail because of trauma, irritation, or maceration. Furthermore, occlusion of the skin with nonporous materials can interfere with the skin's barrier function by increasing local temperature and hydration.[2] With inhibition or failure of the skin's protective mechanisms, cutaneous infection may occur.

Microsporum, Trichophyton, and Epider-mophyton species are the most common pathogens in skin infections. Less frequently, superficial skin infections are caused by nondermatophyte fungi (e.g., *Malassezia furfur* in tinea [pityriasis] versicolor) and Candida species. This article reviews the diagnosis and treatment of common dermatophyte infections.

Older age is also characterized by the emergence of several complex health states that tend to occur only later in life and that do not fall into discrete disease categories. These are commonly called **geriatric syndromes**. They are often the consequence of multiple underlying factors and include frailty, urinary incontinence, falls, delirium and pressure ulcers.

Geriatric syndromes appear to be better predictors of death than the presence or number of specific diseases. Yet outside of countries that have developed geriatric medicine as a speciality, they are often overlooked in traditionally structured health services and in epidemiological research. The present review deals with dermatophytosis in geriatric population.

I. INTRODUCTION

Various factors unique to elderly patients such as physical, physiological, psychological, and socioeconomic factors affect the outcome of dermatophytic infection and its management. The associated comorbidities such as renal and hepatic failure and polypharmacy influence the pharmacological properties of antifungal agents. These drugs are potent inhibitors of hepatic enzymes involved in drug metabolism leading to accumulation and subsequent toxicity of various classes of drugs. All these factors are considered in the management of dermatophytosis in elderly especially with comorbidities. [1]

The management of dermatophytosis has become a big concern owing to various factors related to host, causative agent, and environment. Antifungal therapy in elderly and in those with systemic comorbidities is very challenging because of restricted therapeutic options available for dermatologists. Literature on the management of dermatophytosis in elderly is limited. In general, pharmacotherapy in elderly patients is limited by physical, physiological, psychological, and socioeconomic factors. The presence of comorbid diseases and associated polypharmacy predispose them to recurrent fungal infections and significant drug interactions. Similar challenges are encountered in patients with renal or hepatic dysfunction. A thorough knowledge of pharmacokinetic and pharmacodynamic characteristics of antifungal agents and associated potential drug interactions is essential for successful management of dermatophytosis in such clinical scenarios.[2]

Old-age, comorbid diseases including renal and hepatic disorders with inherent immunological alteration and their treatment influence the manifestation of dermatophytic infection. Dermatophytosis including onychomycosis constitutes about 16% of total cutaneous diseases in elderly patients attending dermatology clinic, and up to 23% in the elderly diabetic. Among dermatophytoses, tinea pedis, and onychomycosis are more common in elderly, especially in males. Onychomycosis has been diagnosed in nearly half of patients presenting with abnormal nails. Distal and lateral subungual are the most common types and *Trichophyton rubrum* and *mentagrophyte*, the common causative organisms. The prevalence of onychomycosis increases with age, with more than 20% occurrence in those above 60 years of age.[3]

The drug-induced immunosuppression in renal transplant patients put them at increased risk of dermatophytic infections, compared to other renal disorders. Dermatophytosis has been reported in 42% renal transplant patients, with tinea cruris and corporis being the common clinical types. The lesions tend to be noninflammatory, scaly and without central clearing, and spread rapidly and extensively following renal transplant.Deeper dermal dermatophytosis presenting as papules, nodules, abscesses, and erythematous plaque has been reported in these patients. Patients with chronic kidney disease are also susceptible to dermatophytic infections especially onychomycosis. In patients on hemodialysis, onychomycosis is the second most common disease involving nails. In patients of end-stage renal disease (ESRD), dermatophtytosis is common in those with underlying diabetes than other conditions. The risk of dermatophytosis is not associated with duration of the evolution of ESRD or hemodialysis. There has been no difference between patients with ESRD and those with normal renal function in relation to organisms isolated and their susceptibility to azoles and terbinafine.[4]

Extensive deep dermatophytosis involving hair follicles and dermis caused by *T. rubrum* has been reported in patients with liver cirrhosis. These patients presented with dermal nodules and purpuric rashes to hemorrhagic nodules. Onychomycosis has been reported as the most common nail changes that occur in patients with hepatic failure constituting 18% of cases. [5]

II. DISCUSSION

Various factors unique to old age such as physiological changes, comorbidities including renal and hepatic failure, polypharmacy, and limitations in personal care need to be considered before choosing appropriate therapy. The extent and site of infection also need to be considered.[6]

Dermatophytosis - types and extent

As in other age-groups, extensive disease and the involvement of palms, soles, and nails requires treatment with systemic antifungal agents. Even in limited involvement, the presence of comorbidities is an indication for systemic drugs.

Physiological changes occurring during dermatophytosis in geriatric population

The secretary function of sebaceous and sweat glands decrease with age, leading to dry skin, which may be the reason for less prevalence of extensive dermatophytosis in elderly. The glomerular filtration rate decreases naturally at the rate of approximately 1 ml/min/year after the age of 30 years as a part of senescence. It is an important factor to be considered while prescribing drugs with predominantly renal excretion.

Comorbidities or multiple diseases in elderly

Elderly individuals commonly suffer from multiple diseases affecting various organ systems. This can lead to immunosuppression predisposing them to cutaneous and systemic infections. Elderly diabetics have 2–3-folds increased risk of onychomycosis compared to nondiabetics.[7]

Drug interactions in geriatric population

Comorbidities in elderly lead to polypharmacy which is associated with significant clinically relevant drug interactions with antifungal agents. This can be due to either pharmacodynamic or pharmacokinetic alterations, the former results from the effect of both drugs on the same physiological process and the latter is commonly mediated by inhibition or induction of hepatic cytochrome enzyme system, which is difficult to predict due to individual variability in response. The effects of drugs on hepatic enzyme system are obvious only when given orally because the drugs have to enter liver during the first pass before entering the systemic circulation. Azoles compete for the cytochrome P-450 (CYP) enzyme, a principle drug metabolizing enzyme in humans, and decrease the elimination of drugs that are metabolized by this enzyme system. The subsequent elevated blood levels of drugs increase the pharmacological effects and dose-

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dependent toxicity. Ketoconazole is found to be the strongest inhibitor of CYP3A4. Itraconazole is potent and fluconazole is the weakest inhibitor among all azoles. However, fluconazole inhibits the enzyme in higher doses. The azoles interact with myriad group of drugs. Hence, proper precaution and careful monitoring of drug levels and toxicity are important when the clinical situation necessitates the concomitant use of azoles (especially ketoconazole and itraconazole) and drugs metabolized by CYP3A4. Terbinafine has no significant drug-drug interaction[8]

Special care for geriatric patients

The elderly patients are usually dependent on caretakers for personal care because of musculoskeletal ailments and age-related forgetfulness. Hence, complex antifungal therapy with topical agents can affect the compliance and may not be feasible in the majority of patients.

III. MANAGEMENT STRATEGY AND TREATMENT

In elderly or geriatric patients

A shorter duration of therapy with efficient antifungal agents is ideal. Terbinafine with clinically insignificant drug interactions seems more rational than azoles in an elderly patient taking multiple drugs for various comorbid diseases. Itraconazole is better avoided in patients on other drugs metabolized by CYP-450 3A enzyme system. The choice of drug, route of administration, dosage and duration of treatment is same as in antifungal therapy in other age groups. However, there are certain factors in elderly which indicate poor response to therapy or increased rate of recurrence. Griseofulvin is not recommended because of low cure rates, high relapse rate, and prolonged daily dosage regimen, especially in onychomycosis[9]

In renal failure occurring in geriatric cases

The determinants of treatment include comorbidities, polypharmacy, and type and extent of dermatophytic infection. The degree of renal insufficiency, causative organisms, and pharmacokinetic properties of antifungal agents need consideration. Only fluconazole and flucytosine are excreted renally as unchanged drug or active metabolites. Terbinafine is excreted primarily through renal systems. In patients with decreased creatinine clearance, fluconazole, and terbinafine require dose adjustment. The terminal half-life of terbinafine and fluconazole increase in patients with renal impairment. Hence, in patients with creatinine clearance <50 ml/min their doses are to be halved

In hepatic failure occurring in geriatric cases

It is also associated with defective host immune response, comorbidities, and polypharmacy. In general, liver diseases that affect hepatic blood flow, protein binding, and enzyme activity significantly alter drug pharmacokinetics. All except cirrhosis cause only mild alterations in hepatic drug clearance. Itraconazole, ketoconazole, and terbinafine are known to cause acute liver failure. The relative risk (RR) of causing acute liver injury being highest with ketoconazole (RR-228), followed by itraconazole (RR-17.7) and terbinafine (RR-4.2). Hence, these drugs should be avoided in patients with hepatic impairment. Griseofulvin is not indicated in patients with hepatic failure. Concomitant alcohol intake, elderly patients, drugs with significant hepatic metabolism and daily dosage of drug exceeding 50 mg are the risk factors for drug-induced hepatotoxicity [10]
The dermatophytosis in elderly and in patients with renal or hepatic impairment can be managed successfully by choosing an appropriate antifungal agent based on patient characteristics, pharmacokinetic, and pharmacodynamics properties, and potential drug interactions. Clinical monitoring of drug toxicity and drug levels is important during antifungal therapy.

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