Editorial

Emerging antifungal treatment failure of dermatophytosis.

Fungal skin infections are one of the most common skin ailments in Bangladesh. For years together, treatment of these conditions was not that difficult. In most cases, topical anti-fungal preparations alone or in combination with oral antifungals were sufficient to combat the diseases. But for the last few years, treatment failure in terms of nonresponse, delayed response, and recurrence emerged with a great threat to the physicians and a matter of enormous suffering for the patients. Dermatologists are also facing the challenges of dermatophytosis involving larger areas of the body and concomitant infection of several members of a family.

The World Health Organization reported up to 19.7% prevalence of dermatomycoses in the general population of developing countries.[1] Superficial mycosis is among the most frequent forms of human infections affecting more than 20-20.5% of the world's population.[2] However, in recent years, these infections have become recalcitrant to treatment which can possibly be due to antifungal resistance. Recalcitrant dermatomycosis refers to relapse, recurrences, reinfection, persistence, and possibly microbiological resistance.[3]

Dermatophytes are classified under three genera namely Trichophyton, Epidermophyton, and Microsporum. Despite the availability of a wide range of antifungal drugs for dermatophytosis, treatment failure has been reported worldwide. This might be due to non-compliance of patients, patient co-morbidities (immunosuppression, diabetes mellitus), inappropriate drug administration, discontinuation of therapy, and infection with non-dermatophyte fungi that are non-responsive to antifungal treatment (Scopulariopsis, Fusarium, and Neoscytalidium sp.).[4-5]

Many topical and oral antifungal drugs are recommended for the treatment of dermatophyte infection, but over time, an increased number of treatment failure cases are appearing. The possible cause for treatment failure could be poor patient compliance, poor drug penetration into the affected lesions, and also drug resistance in dermatophytes.[6] Azoles and allylamines including fluconazole, itraconazole, and terbinafine are the frequently prescribed systemic antifungals.

Although there is an increasing rate of relapse cases of dermatophytosis are reported, but these have not been conclusively proven to be a consequence of resistance. We should consider few different issues behind this relapse or treatment failure which includes altered epidermal defense, host immunity, irrational use of topical steroid and use of mixed preparation of antifungal with topical corticosteroids.[7]

The resistance of an antifungal drug could be considered in case of failure to eliminate the lesion or reappear within four weeks of a complete course of therapy with a standard dose.[8] Antifungal susceptibility testing (AFST) is a reliable tool to decide the most effective drug against a particular dermatophyte or to label a drug as "resistant' when it fails to respond. AFST determines the minimum inhibitory concentration (MIC) value which is used to develop treatment protocol, designing epidemiological studies, and follow the track of antifungal resistance.[9] This is based on the skin pharmacokinetics (pk) of the major drugs used in dermatophytosis. It is noteworthy that AFST is not being carried out routinely in dermatophyte infections. After administration of terbinafine 250 mg daily for 12 days, drug concentrations above the Minimum Inhibitory concentration (MIC) for most dermatophytes may persist for 2–3 weeks after oral therapy is discontinued.[8] Itraconazole may persist in the stratum corneum for 3–4 weeks after discontinuation of therapy.[10-11] Thus, an infection that recurs within 4 weeks after adequate oral therapy can be due to resistance, though the additional role of immune compromisation cannot be ruled out.

Aktas et al. found no resistance of oral terbinafine and itraconazole with a maximum MIC level of 1 µ g/ml, whereas fluconazole had shown resistance with a higher MIC.[12] Moreover an MIC90 same to terbinafine was found for amphotericin B which open a possibility to use it as a topical agent for dermatophyte infections.[12] Voriconazole showed

the lowest MIC from 0.002 to 0.06 µg/m, but its variable metabolism is a concern for toxicity or therapeutic failure.[13]

So, it is the prime time to conduct a series of clinical, epidemiological, and laboratory-based studies to find out the particular causative fungus, effective antifungal drugs, the pattern of resistance, MIC of different antifungal to different dermatophyte, and dosage-duration of treatment. Based on these data a local guideline of dermatophytosis management can be developed to confront the situation.

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