Amorolfine, a Breakthrough in Topical Antimycotic Therapy

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Summary

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During the course of this symposium the preclinical, pharmacological and therapeutic repertoire of the new morpholine antifungal agent, amorolfine, has been introduced. This compound is active in vitro against the causative agents of most of the superficial mycoses, from dermatophytosis to candidosis and shows fungicidal activity in vitro against many of the same organisms. This in vitro activity is mirrored by responses in both experimental infections in animal models as well as in the early dose ranging studies of human dermatophytosis and superficial candidosis. The drug also appears to have a long retention time on the surface of the epidermis, which may prove advantageous in preventing relapse. Ultrastructural studies of fungi treated with amorolfine have shown that, in common with the azole antifungals, there is extensive disruption of the cell with vacuole and lipid droplet formation and, in the case of dermatophytes, gross thickening of the cell wall.

Studies of the penetration of the drug through nail show that therapeutic concentrations of amorolfine in a variety of suitable bases, the most effective being DMSO, can be found on the other side of the excised nail plate after application to the superior surface. A multicentre study of topically applied 5% amorolfine nail lacquer confirmed that clinical and mycological remissions were achieved in 46% of patients applying the drug once weekly for up to 6 months and 54% of those applying the preparation twice weekly for the same period in a large study of 456 patients. Less than 1% reported irritant side effects.

While there are a number of highly active topical antifungals currently available, the development of a cidally active compound is clearly to be welcomed as it is likely to reduce the duration of therapy and frequency of relapse. These early studies confirm that amorolfine is clinically effective in the treatment of a variety of superficial mycoses and demonstrate that it is possible to produce remissions of fungal nail disease using topical therapy alone. The past history of the use of topical therapy in the management of onychomycosis, apart from paronychia, has not been satisfactory and amorolfine appears clearly to represent an advance in this field, provided that the long-term relapse data confirm that permanent cures do occur. It is to be hoped that, subsequently, the minimal durations of therapy will be defined in order to reduce the length of treatment even further in a variety of different fungal infections and to determine the best regimen for optimal application of the drug in the management of onychomycosis.

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