The Interaction between Stratum Corneum and Dermatophytes in Patients with Chronic Tinea Pedis

Sir,

It has been found that the frequency of dermatophyte infections, confirmed by mycological culture in patients suffering from hereditary palmo-plantar keratoderma (HPPK), is rather high (36.7%) (1). Gamborg Nielsen & Faergemann (2) found that stratum corneum from patients with HPPK inhibits the growth of Trichophyton rubrum in cultures. In this study, we wanted to examine if the stratum corneum from patients free from HPPK but clinically suffering from chronic tinea pedis had a similar effect on T. rubrum.

MATERIAL AND METHODS

Characteristics of the patients

Thirteen patients suffering from chronic tinea pedis, with positive cultures of T. rubrum, were included in the study. They had not been treated with oral or topical antifungal for at least 2 months before they entered the study. Controls were either individuals without any skin diseases or patients with minor skin tumors, such as nevi, but without any signs of dermatomycosis. These 6 controls were all men aged 31 to 58 years. They were all free from drugs.

Collection of stratum corneum

Stratum corneum was collected by curetage from both soles of patients and controls.

Collection of fungi

Specimens for fungal culture were collected by scraping the affected skin of the sole with a curette and inoculated on casein agar, containing powdered skin milk, yeast extract, actidione, chloramphenicol, gentamicin, agar, bromocresol purple and distilled water, at 32°C for 1 month; they were then kept at 25°C and reinoculated on casein agar every month for no longer than 5 months. The dermatophytes were identified macroscopically and microscopically. Microscopic examination was performed using a sterile plastic loop to collect the dermatophyte onto a glass slide stained with lactophenol cotton blue.

A laboratory dermatophyte culture of T. rubrum from the Mycological Laboratory, Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden, served as a control culture.

Experimental procedure

Curettaged stratum corneum from patients and controls was sterilized with ethylene gas (3). Dermatophytes isolated from patients with chronic dermatophytosis were harvested in sterile plastic tubes containing phosphate-buffered saline (pH 7.2) and crushed with a glass rod. The suspensions were then filtered through filter gauge and adjusted to an optical density of 65% (range 62–70%) transmission at a wavelength of 559 nm (Beckman Model 24 Spectrophotometer). From these solutions, 0.3 ml was inoculated on Sabouraud’s glucose agar without cycloheximide. Sterilized stratum corneum from the soles of the corresponding patients was then placed in the center of one half of the plate and sterilized stratum corneum from the soles of a matched control in the center of the other half of the plate. As a control, one plate with stratum corneum from both one patient and one healthy subject was inoculated with a laboratory dermatophyte. The growth of the dermatophyte in relation to the inoculated stratum corneum was recorded. Inhibition of growth of the dermatophyte was assessed by measuring the zone of reduced growth or total inhibition around the inoculated stratum corneum.

RESULTS

Of the 13 patients, 7 were excluded because too small an amount of stratum corneum could be sampled from their soles. The final number of patients was 6, all men (age 43–68 years). Inhibition of growth of T. rubrum was seen around stratum corneum in 4 patients and one healthy control. However, growth was only totally inhibited by stratum corneum from 2 patients. In these 2 patients there was an inhibition zone of at least 8 mm. In 2 other patients and one healthy control, reduced growth was observed around the stratum corneum, but there was no total inhibition. In these 3 individuals, growth was normalized after 5 to 12 days. In all cultures where no inhibition of T. rubrum was present, growth was seen on the whole culture plate, including the area inoculated with stratum corneum.

DISCUSSION

T. rubrum is the dermatophyte most commonly involved in chronic dermatophyte infections, including tinea pedis. Why some individuals develop chronic dermatophyte infections is still not known. We know there are hereditary factors involved in chronic tinea pedis (CPD). Delayed type hypersensitivity (DTH) is an essential part of the defense against infections with dermatophytes (4, 5). The T-cell derived cytokine IFN-γ plays a major role in the effector phase of the DTH reaction (6).

Stratum corneum from several patients with HPPK and CTP had an inhibitory effect in vitro on dermatophytes instead of stimulating the growth, as expected (2). Adherence of microorganisms to stratum corneum cells is the initial mechanism for both colonization and infection. Many fungi will alter the initial adherence start to produce hyphae. However, in the present investigation we found, as in the study with HPPK and CTP, an inhibitory effect of stratum corneum on T. rubrum. This indicates that there could be factors not only in patients with HPPK but also in patients with CTP alone that can inhibit the growth of dermatophytes in vitro. Inhibition by stratum corneum from patients with chronic T. rubrum infection points to an immunologic reaction to dermatophytes in many of these patients. The fact that T. rubrum can still infect these patients can be explained by in vivo factors that support the growth of T. rubrum, for example the presence of other microorganisms, or substances which neutralize the inhibitory substances and which are destroyed under in vitro conditions. However, further investigations are necessary to clarify this.

REFERENCES


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Cycloheximide in Dermatology

Sir,

Although cycloheximide (CHM) or Actidione®, isolated from Streptomyces griseus, is an antibiotic widely employed in the laboratory, its clinical use has been limited. Because of the great deal of information which indicates that this drug has therapeutic value as a topical agent, we wish to present the dermatological data presently available. Its molecular formula is C_{13}H_{13}N_{2}O_{4}.

BIOCHEMICAL PROPERTIES

CHM inhibits the synthesis of protein and DNA (1). The inhibitory effects on mammalian cells are reversible, often a desirable property from a therapeutic standpoint. CHM specifically inhibits the function of 80S ribosomes and enhances the endotoxin-induced production (superinduction) of interferon (2).

MEDICAL USE

CHM has been administered intramuscularly, intravenously and intrathecally to treat mostly cryptococcosis patients in daily doses ranging from 10 mg to 60 mg. One patient received 2.681 mg intramuscularly in one day without toxicity. A total of 175 individuals have received the drug with excellent tolerance.

DERMATOLOGICAL USE

Psoriasis

Topical CHM (0.1–0.2%) dispersed in Aquaphor® produces involvation of psoriatic plaques (3). In our clinic a phase-II double-blind, tolerance-efficacy comparison of CHM versus vehicle applied b.i.d. showed a statistically significant superiority of CHM over the vehicle. There was no systemic or local toxicity.

In the national multicenter cooperative study undertaken by Weinstein and twelve other leading U.S.A. investigators (4) to evaluate the clinical effectiveness of 30 topical anti-psoriatic agents, CHM was ranked among the seven leading compounds.

Cutaneous malignancies

Du Vivier (5) employed 1% CHM b.i.d. to treat actinic keratoses, superficial basal cell carcinomas and Bowen’s disease.

Clinical and histopathological cure, including disappearance of lesions previously resistant to 5-fluouracil, was observed.

Human papillomavirus

Plantar warts, verrucae vulgaris and condylomata acuminata were treated in our clinics with excellent response using 0.2% CHM dispersed in Aquaphor®. The ointment was rubbed b.i.d. with a cotton-tipped applicator until complete penetration was obtained or applied once daily under occlusion.

Parakeratosis

Shelley & Shelley (6) obtained dramatic improvement in the treatment of a linear parakeratosis which had resisted a large variety of therapies over 11 years, using 0.2% CHM in Aquaphor® once daily for 6 weeks.

COMMENTS

Although CHM has shown efficacy and lack of toxicity in a number of dermatological conditions treated by several investigators, it falls within the category of an orphan drug because it still lacks an approved indication. Performance of additional controlled topical trials in various dermatoses and systemic evaluations in a number of diseases, especially viral infections, appear justified.

REFERENCES


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