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EFFECT OF A SINGLE DOSE OF R126638 IN SEBORRHEIC DERMATITIS

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Introduction: R126638 is a novel azole with antifungal activity, especially against *Malassezia* spp.—related diseases.

Objective: To evaluate whether oral treatment with R126638 was effective in reducing the number of live *Malassezia* yeasts on the forehead of patients with seborrheic dermatitis. The effect on clinical symptoms like desquamation, erythema, itching, and sebum secretion was also studied.

Methods: Ten patients with seborrheic dermatitis were allocated for treatment with a single oral dose of 200 mg R126638. Skin strips (D-squame) of the forehead were taken to determine (1) the area of scales (mm^2), (2) the number of living yeasts (by neutral red staining), and (3) the number of living yeasts per area of scales. For clinical evaluation a visual appraisal of desquamation was performed, itching was scored on a visual analogue scale, sebum secretion was assessed by measuring the number and total area of spots using Sebux combined with Visiocsan, scaliness was measured with Chroma C of D-squames, erythema was measured by colorimetry with the Minolta Chromameter. The mycological and clinical evaluations were performed before and after 3, 7, and 28 days of treatment.

Results: The mycological parameters were reduced at all visits; a statistical significant effect compared with baseline was seen on the number of living yeasts and the number of yeasts/ mm^2 scales at days 3, 7, and 28 was seen. The clinical parameters scaliness severity, desquamation, erythema, itching, and global clinical evaluation by the patient and the investigator were not significantly reduced at day 3. All these clinical parameters were significantly reduced at day 7 and 28, with the exception of scaliness. As expected, an effect on sebum secretion was not achieved. These data indicate that after reduction of the number of yeasts at day 3, a decrease in the severity of clinical symptoms occurs from day 7 onward.

Conclusion: This proof of concept study suggests that R126638 possesses properties that warrant further investigations for its use in the treatment of seborrheic dermatitis.

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EFFECTS OF SERTAONAZOLE NITRATE ON T-CELL ACTIVATION, IRRITANT DERMATITIS, AND CONTACT HYPERSENSITIVITY

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Sertaconazole nitrate is a broad-spectrum antifungal compound that is efficacious against dermatophytes, yeast, and some gram-positive bacteria. In addition to the antifungal activity, sertaconazole nitrate is well suited for topical administration with a good safety profile, low systemic absorption, and a long-lasting cutaneous retention. Since cutaneous fungal infections are often manifested as irritated skin, studies were conducted to evaluate the activity of sertaconazole nitrate on inflammatory pathways associated with irritated skin.

Sertaconazole nitrate inhibited the release of the Th1 cytokines interleukin 2 (IL-2) and interferon- γ , the Th0/Th1 cytokine tumor necrosis factor- α , and granulocyte-macrophage-colony-stimulating factor from activated human lymphocytes with IC50s of 35, 5, 6, 7 $\mu\text{g/mL}$, respectively. Sertaconazole nitrate also inhibited the proliferation of stimulated human lymphocytes with an IC50 of 4 $\mu\text{g/mL}$. No toxicity was observed at any concentration of sertaconazole nitrate tested.

The irritation potential of a sertaconazole nitrate cream was assessed using human skin equivalents *in vitro*. After 24-hour treatment with a cream containing 2% sertaconazole nitrate, there was no significant release of proinflammatory cytokines IL-8 or IL-1 α and no loss of tissue viability, indicating that sertaconazole nitrate is nonirritating.

In vivo efficacy was examined in two murine dermatitis models. Topical administration of sertaconazole nitrate inhibited phorbol ester-induced irritant dermatitis with an ED50 of 1%. Topical treatment with Sertaconazole Nitrate was also effective against contact hypersensitivity, reducing edema in oxazolone-challenged mice with an ED50 of 2%. Furthermore, sertaconazole nitrate was more effective in reducing dermal irritation than other azole compounds tested.

Sertaconazole nitrate is used topically in a 2% formulation for the treatment of tinea pedis, which is comparable to the effective dose of the compound to reduce irritation. Taken together, these results demonstrate that sertaconazole nitrate has anti-inflammatory activity that may contribute to the treatment of cutaneous fungal conditions.

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EPIDEMIOLOGY AND TREATMENT OF ONYCHOMYCOSIS BASED ON THE NATIONAL AMBULATORY MEDICAL CARE SURVEY, 1990-1999

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The National Ambulatory Medical Care Survey (NAMCS) has collected nationwide outpatient data from U.S. non-federally employed physicians for more than 20 years. We analyzed data from 316,928 visits, which when weighted estimated the experience of 7.3 billion physician visits between 1990 and 1999. The collection of data by the NAMCS provides an opportunity to look at a wide range of populations in the United States, over a significant time period, to provide an estimate of onychomycosis infection and treatment.

Onychomycosis is represented in the NAMCS by the ICD-9 code 110.1 (dermatophytosis of the nail). In the years surveyed, the number of cases of onychomycosis predicted is 7.47 million (0.10% of all NAMCS visits). This percentage is much lower than national estimates made for onychomycosis in other studies, suggesting that many people do not seek treatment for onychomycosis. However, from 1990 to 1999, the percentage of onychomycosis diagnoses made increases from 0.05% to 0.17%, suggesting that in the past 10 years, the number of people seeking treatment is increasing. Dermatologists were treating 45% of these onychomycosis cases.

Of the oral antifungal agents used to treat onychomycosis, terbinafine and itraconazole are rather recent medications. Up to 5 or 6 medications could be specified in the NAMCS data, depending on the year of the survey. Five-digit medication codes were provided in the NAMCS, but did not indicate conclusively that the formulations coded were for oral use (terbinafine: "lamisil-93243"; itraconazole: "sporonox — 93222"; griseofulvin: "grifulvin-13785," "griseofulvin-13800"). Although overall in the NAMCS dataset griseofulvin is used in only 7% of primary cases of onychomycosis, in 1993 the usage was at a high of 34.5%. Terbinafine and itraconazole begin appearing in the NAMCS data in 1993 and 1994, and in 1998, all 3 agents had similar usage rates, between 20% and 27%. The use of these agents shows high variation in rates of use between 1999 and 1999. There is no obvious explanation for the inconsistency of treatment use.

Use of the NAMCS data to provide an estimation of treatment for onychomycosis must be further investigated. This preliminary analysis may not have captured all drug codes representing the oral antifungal agents and does not capture any topical medications provided.

Nothing to disclose.

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EPIDEMIOLOGY OF DERMATOPHYTOSIS AND PITYRIASIS VERSICOLOR IN THE UNITED STATES, BASED ON THE NATIONAL AMBULATORY MEDICAL CARE SURVEY, 1990-1999

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Determining national prevalence rates of medical conditions is difficult because large-scale surveys are costly and time-consuming to organize. The National Center for Health Statistics has collected nationwide outpatient data from U.S. non-federally employed physicians for more than 20 years in the National Ambulatory Medical Care Survey (NAMCS). Data from 1990 to 1999 were collected from the NAMCS survey and used to generate estimates of the rates of dermatophytosis in the United States during these years.

We analyzed data from 316,928 visits, which when weighted estimated the experience of 7.3 billion physician visits between 1990 and 1999. Dermatophytosis (infection by species of *Epidermophyton*, *Microsporum*, and *Trichophyton* tinea) is captured in the NAMCS dataset as an ICD-9 diagnosis code of 110.0-110.9. Pityriasis versicolor was also considered and is presented in the NAMCS as an ICD-9 code of 111.0.

Dermatophytosis or pityriasis versicolor was found in 0.46% of a possible 7.3 billion visits modeled by the NAMCS data. This analysis considered cases in which dermatophytosis or pityriasis versicolor was the primary diagnosis made at the visit. Of the primary fungal infection diagnoses considered, 94% of these cases were the sole diagnosis made at the visit. The most frequent dermatophytosis infection specified was dermatophytosis of the body (22%), followed by dermatophytosis of the nail (19%), dermatophytosis of unspecified sites (16%), dermatophytosis of the foot (12%), and dermatophytosis of the groin/perianal region (10%). Pityriasis versicolor was found in 9% of primary diagnoses of fungal infection surveyed. The distribution of infections noted among the regions of the United States surveyed (Northeast, Midwest, South, and West) was similar. Dermatologists diagnosed only 29% of cases in which a primary diagnosis of dermatophytosis was made, suggesting that family physicians or other specialists are treating a majority of dermatophytosis cases in the United States. For nondermatologists, the predominant dermatophytosis diagnosis made was dermatophytosis of the body (22%). In contrast, dermatophytosis of the nail is the predominant primary dermatophytosis diagnosis made by dermatologists (27%), which may suggest that dermatologic expertise is sought in fungal presentations that are known to be more difficult to treat.

Nothing to disclose.