Infants at risk but even less-promising results regarding its use in the treatment of AD. This study adds to the literature, finding no utility of lactobacilli supplementation for the treatment of established AD.

Corinne A. Keet, MD
Robert A. Wood, MD
Baltimore, MD

Intermittent Therapy for Flare Prevention and Long-term Disease Control in Stabilized Atopic Dermatitis: A Randomized Comparison of 3-Times-Weekly Applications of Tacrolimus Ointment Versus Vehicle

PURPOSE OF THE STUDY. To examine the usefulness of regular intermittent therapy instead of treating flares for the approach of atopic dermatitis (AD).

STUDY POPULATION. A total of 383 patients were randomly assigned to the stabilization phase, and 288 patients were controlled on tacrolimus ointment. There were 68 children (aged 2–16 years) and 57 adults (>16 years) in the tacrolimus arm and 37 children and 35 adults in the vehicle arm. Eighty-five percent had moderate AD, and 15% had severe AD.

METHODS. Adult and pediatric patients with moderate-to-severe AD who were clear of disease after up to 16 weeks of treatment with tacrolimus ointment were randomly assigned in a double-blind fashion to 3-times-weekly treatment with either tacrolimus ointment (0.03% or 0.1%) or vehicle for 40 weeks. The primary end point was the number of flare-free treatment days. Relapses were treated with open-labeled tacrolimus.

RESULTS. There were 288 patients who entered the randomization phase. The largest reasons for not finishing the stabilization phase were voluntary patient withdrawal for 95 patients and loss to follow-up for 55 patients. Only 16 (4.2%) patients were withdrawn for lack of efficacy. A total of 125 patients were randomly assigned to tacrolimus, and 72 patients were assigned to vehicle. The mean number of flare-free treatment days was 177 for the tacrolimus group and 134 for the vehicle group (P = .003). Median time to first relapse was 169 days for the tacrolimus group and 43 for the vehicle group (P = .037).

CONCLUSIONS. Maintenance therapy with tacrolimus ointment was associated with significantly more flare-free days compared with vehicle and a significantly longer time until first disease relapse.

REVIEWER COMMENTS. This article examined the possibility of proactive treatment of AD instead of reacting to flares.

Sustained Efficacy and Safety of Pimecrolimus Cream 1% When Used Long-term (up to 26 Weeks) to Treat Children With Atopic Dermatitis

PURPOSE OF THE STUDY. To evaluate the efficacy and safety of pimecrolimus cream 1% (Elidel [Novartis, East Hanover, NJ]) used for 26 weeks in children with atopic dermatitis (AD).

STUDY POPULATION. This was a prospective study of 403 children aged 2 to 17 years with AD (mean age at enrollment: 6.7 years) recruited from multiple academic centers in the United States.

METHODS. Pooled data were assessed from 20-week, open-label (OL) extensions of 2 previously reported 6-week, double-blind (DB) phase studies in which patients were randomly assigned 2:1 to pimecrolimus or vehicle. During the OL phase, all patients were treated with pimecrolimus. During the DB phase, no other AD treatments except emollients were allowed. The efficacy parameters included the Investigator’s Global Assessment (IGA), Eczema Area and Severity Index, and severity of pruritus scores. Safety assessment consisted primarily of monitoring adverse events. Patients were evaluated on days 8, 15, 22, 29, 43, 71, 99, 141, and 183.

RESULTS. Overall, 60.3% of the patients had moderately severe AD (IGA: 3) at study entry. Twice as many in the control group discontinued during the DB phase compared with the treated group (25% vs 11.4%). The main reason for the higher discontinuation rate in the control group was unsatisfactory therapeutic effect (15.4% vs 2.6%). Eighty-four percent completed the OL phase with similar rates of completion between the groups. At day 43, 34.8% of the pimecrolimus-treated patients versus 18.4% in the vehicle groups (P < .001) had clear or almost clear (IGA: 0 or 1) disease. Pimecrolimus was significantly more effective (P < .0001) in treating the
face and neck compared with the body during both DB and OL phases. In the pimecrolimus group, 56.5% of the patients had mild or absent pruritus by day 43 compared with 33.8% of those in the control group. The incidence of adverse events, including infections and complaints of a burning sensation with application, was not statistically different between groups during either phase of the study.

CONCLUSIONS. Treatment of AD with pimecrolimus was effective, particularly for the face and neck areas, and well tolerated.

REVIEWER COMMENTS. Given the black-box warning and concern with using topical calcineurin inhibitors, this article reemphasized that pimecrolimus is efficacious for children with AD. Particularly, it should be considered for use on the face and neck, which are difficult to treat with higher potency topical corticosteroids because of the risk of local adverse effects such as atrophy. The minimal adverse events associated with pimecrolimus support previous studies that had longer durations of treatment (up to 2 years).

H1-Antihistamine Treatment in Young Atopic Children: Effect on Urticaria

PURPOSE OF THE STUDY. To evaluate the effect of long-term treatment with levocetirizine on urticaria in young children with atopic dermatitis (AD).

STUDY POPULATION. The group studied 510 children with severe AD disease (mean Scoring Atopic Dermatitis [SCORAD] index: 30) aged 12 to 24 months at enrollment. This study is from the Early Prevention of Asthma in Atopic Children (EPAAC) study.

METHODS. This was a multicenter, randomized, double-masked, parallel-group, placebo-controlled study. Enrolled children were followed for 18 months on treatment with levocetirizine 0.125 mg/kg or placebo twice daily. The occurrence of urticaria was recorded on diary cards by parents or caregivers and “validated” by study investigators (validation was not explained).

RESULTS. During the 18 months of treatment, 27.5% (70 of 255) of the children receiving levocetirizine experienced urticaria in contrast to 41.6% (106 of 255) of the children receiving placebo (P < .001). The mean number of episodes of urticaria was 0.71 ± 0.11 and 1.71 ± 0.25 in the levocetirizine and control groups, respectively (P < .001). Urticaria was noted on a mean of 4.43 days in levocetirizine-treated patients and 5.36 days in placebo-treated patients (P < .001). For 85% of the children, the urticaria lasted ≤7 days. In 77% of the children with urticaria, the outbreak was associated with food ingestion. No significant adverse effects or long-term adverse effects were noted with active treatment.

CONCLUSIONS. Forty-two percent of highly atopic young children in the EPAAC study had acute urticaria, predominantly associated with food ingestion. Levocetirizine was effective at preventing urticarial outbreaks and had a modest effect treating urticaria, as demonstrated by the decrease in the duration of the episodes.

REVIEWER COMMENTS. In a previous, similar trial (Early Treatment of the Atopic Child [ETAC]) in young children with AD treated with cetirizine, acute urticaria was reported in 16% of the patients treated with placebo and 6% of the patients treated with the antihistamine (Simons FE. J Allergy Clin Immunol. 2001;107[4]:703–706). These patients were less highly atopic than the present study. The current EPAAC study is hindered by the lack of explanation of validation of urticarial episodes. This study has extended knowledge on the safety of cetirizine/levocetirizine for young children with AD and their efficacy in preventing acute urticaria resulting from food allergy.

Attenuation of Allergic Contact Dermatitis Through the Endocannabinoid System

PURPOSE OF THE STUDY. To assess the role of cannabinoid receptors in allergic contact dermatitis.

STUDY POPULATION AND METHODS. The study was conducted in an animal model for cutaneous contact hypersensitivity using wild-type mice and also those lacking cannabinoid receptors (CB1 and CB2).

RESULTS. Mice lacking both known cannabinoid receptors display exacerbated allergic inflammation. In contrast, fatty acid amide hydrolase–deficient mice, which have increased levels of the endocannabinoid anandamide, displayed reduced allergic responses in the skin. Cannabinoid receptor antagonists exacerbated allergic inflammation, whereas receptor agonists attenuated inflammation.
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