

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).

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Audrey Y. Park, MD, PhD
Jonathan M. Spergel, MD, PhD
Philadelphia, PA

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

Simons FE; Early Prevention of Asthma in Atopic Children Study Group. *Ann Allergy Asthma Immunol.* 2007;99(3):261–266

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.

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Alan B. Goldsobel, MD
San Jose, CA

Attenuation of Allergic Contact Dermatitis Through the Endocannabinoid System

Karsak M, Gaffal E, Date R, et al. *Science.* 2007;316(5830):1494–1497

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.

CONCLUSIONS. These results demonstrate a protective role of the endocannabinoid system for contact allergy in the skin and suggest a target for therapeutic intervention.

REVIEWER COMMENTS. This very clever study was based on an observation that mice lacking cannabinoid receptors tended to develop an itchy dermatitis at the site of nickel-containing ear tags. From this simple observation, the authors conducted a series of well-designed experiments that demonstrated that the cannabinoid receptors help

to regulate cell recruitment to sites of inflammation in the context of contact dermatitis. These results have led to new insights to the pathogenesis of this disorder and may lead to a new treatment for contact dermatitis. I wonder if cannabinoid receptors are involved in other forms of skin allergy.

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James E. Gern, MD
Madison, WI