rhinitis, and systemic reactions involving hypotension, laryngeal edema, bronchospasm, and/or shock.

METHODS. All subjects completed a questionnaire detailing the implicated NSAID, their reaction history, and any individual risk factors. Subjects were stratified into 2 separate groups: those who reacted to a single NSAID and those who reacted to multiple NSAIDs. Based on a diagnostic algorithm, those with a positive result on skin prick test (SPT) to a single NSAID (n = 1) were labeled as NSAID-H, and those with negative or no available SPT underwent an oral provocation test (OPT). Those with a confirmed history of anaphylaxis did not undergo OPT. Subjects with a history of reaction to ≥2 NSAIDs underwent OPT. Subjects received 4 to 5 escalating doses of the culprit NSAID at 60-minute intervals until they reached the maximum single dose. Patients were observed for 2 hours after the OPT to monitor for delayed reaction. All challenges were continued for 2 days at home, and subjects were contacted via telephone for follow-up. OPTs were performed in all children with confirmed NSAID-H in an attempt to find a safe alternative.

RESULTS. Sixty-five percent (n = 38) reported a reaction to a single NSAID. Thirty-five of these subjects underwent an OPT, and 5 had proven NSAID-H. Of the 20 patients who reported reactions to multiple NSAIDs, 8 had proven NSAID-H with OPT. Twelve patients were challenged to find a safe alternative, of whom 60% tolerated acetaminophen and 89% tolerated nimesulide. There was no association between gender, atopic status, presence of atop disease, history of anaphylaxis, history of multiple reactions with the same NSAID, and safe use of a similar group of NSAD and OPT results. Family history of NSAID-H and having a reaction with multiple NSAIDs were associated with a positive result on OPT.

CONCLUSIONS. A history of reaction to both single and multiple NSAIDs was usually not indicative of true drug hypersensitivity. Therefore, diagnostic tests should be considered in all children with suspected NSAID-H.

REVIEWER COMMENTS. Although suspected allergic reactions to NSAIDs are very common, true allergy is uncommon in children compared with adults. This impression was confirmed in this study, with true allergy confirmed in only ~25% of those reporting a history of reaction. This study also confirms the value in performing provocation tests, and the lack of value in skin testing, in children presenting with a history of a suspected NSAID allergy.

Patterns of Clinical Management of Atopic Dermatitis in Infants and Toddlers: A Survey of Three Physician Specialties in the United States


PURPOSE OF THE STUDY. The goal of this study was to describe atopic dermatitis (AD) management patterns in children aged ≤36 months as reported by pediatricians, dermatologists, and allergists in the United States.

METHODS. A nationally representative survey was administered to pediatricians (n = 101), dermatologists (n = 26), and allergists (n = 26). Main outcomes included referrals to health care professionals, suggested/ordered laboratory tests, and management approaches (dietary, pharmacologic, or combination of both) according to age, AD location, and severity.

RESULTS. Significant differences were observed in referrals to health care professionals (P < .001). Pediatricians more frequently referred children to dermatologists than allergists in mild (52.4% vs 32.0%) and moderate/severe (66.6% vs 38.1%) cases. Dermatologists referred children to allergists less frequently for mild (9.1%) than moderate/severe (40.7%) AD cases. Pediatricians (59%), allergists (61.5%), and dermatologists (26.9%) reported treating at least some of their patients with AD by using dietary management (infant formula change) alone (with or without emollients). Soy-based formulas were often used. For mild AD, the most commonly reported first-line pharmacologic treatments included topical emollients, topical corticosteroids, and barrier repair topical therapy/medical devices. More than 80% of physicians used a dietary and pharmacologic combination approach. Dermatologists were most likely to manage AD symptoms with a pharmacologic-only approach. Location of the AD lesion influenced pharmacologic treatment in >80% of physicians.

CONCLUSIONS. Significant and distinct differences in AD treatment approach exist among the physicians surveyed. Most pediatricians and allergists use formula change as a management strategy in some patients, whereas dermatologists favor a pharmacologic approach.

REVIEWER COMMENTS. This survey highlights the need for a more unified approach to the diagnosis and treatment of this chronic disease, which affects 10% to 20% of children. The investigators concluded that pediatricians and allergists were more likely to use formula change as a management strategy, with allergists specifically more likely to use laboratory tests (eg, IgE, skin prick) or an elimination diet with a food challenge test, and that dermatologists favor a pharmacologic approach to treatment and are less likely to consider food allergy as a cause of AD. A unified approach should be based on the possible etiologies of AD in affected children. This approach requires an understanding of the mechanisms of hypersensitivity to food and some
environmental allergens that are frequent causes of the most severe forms of AD in infants and small children. It also requires knowledge of the benefits and pitfalls of testing for allergies, because not all patients who test positive for a food protein actually have an allergic reaction to that food. Erroneous interpretation of allergy tests can lead to extensive elimination diets that can further complicate the patient’s life and may lead to nutritional problems. Comprehensive management of AD requires a multifaceted approach, including avoidance of allergens and irritants, skin moisturization, topical anti-inflammatory agents, and anti-itch and anti-infection measures.

**Immunologic Effects of Omalizumab in Children With Severe Refractory Atopic Dermatitis: A Randomized, Placebo-Controlled Clinical Trial**


**PURPOSE OF THE STUDY.** Case reports on the benefit of anti-IgE therapy in children with atopic dermatitis (AD) have been published. This study is investigating the effect of omalizumab on symptomatic improvement of AD in a randomized, placebo-controlled manner.

**STUDY POPULATION.** Eight patients between the ages of 4 and 22 years (mean age: 11.6 years) with severe, treatment-refractory AD were recruited. Four patients received omalizumab every 2 to 4 weeks for 24 weeks, and 4 patients received placebo at the same time points.

**METHODS.** Blood samples were taken at enrollment. Previous eczema medications were standardized among patients; these medications consisted mainly of cetirizine, triamcinolone, and pimecrolimus. Baseline skin condition and medication use were recorded by the parents in the form of a diary. Baseline serum IgE level was recorded. All medication was discontinued 1 week before the start of omalizumab/placebo. At each monthly visit, AD scoring using the SCORAD (Scoring Atopic Dermatitis) index was performed. In addition, quantitative serum IgE levels and relevant cytokines were measured at each visit.

**RESULTS.** All patients had markedly elevated AD scores at baseline. Baseline serum IgE ranged from 218 to 1890 IU/mL (mean: 1068 IU/mL). SCORAD reductions of 20% to 50% were noted in the omalizumab-treated group; however, a 45% to 80% reduction was noted in the placebo group. Patients who received omalizumab had significant decreases in free serum IgE levels. Cytokines measured at monthly intervals showed reduction of relevant cytokines and markers in the omalizumab-treated group (TSLP, TARC/CCL17, OX40L, and IL-9). IL-10 levels were noted to be increased in the omalizumab-treated group.

**CONCLUSIONS.** No difference in clinical symptoms score could be seen. Significant changes in molecular biomarkers were noted in the omalizumab-treated group. A larger, randomized, placebo-controlled trial would be necessary to examine the effects on antigen-specific, T-cell proliferation and function.

**REVIEWER COMMENTS.** This very small pilot study reported the expected effect of omalizumab on quantitative IgE levels and cytokines. Clinical symptom change was not different between the groups. A larger trial is needed to assess the role of IgE in AD.

**The Epithelial Cell-Derived Atopic Dermatitis Cytokine TSLP Activates Neurons to Induce Itch**


**PURPOSE OF THE STUDY.** Atopic dermatitis (AD) is a cutaneous disorder characterized by inflamed and pruritic (itchy) skin. The proallergic cytokine thymic stromal lymphopoietin (TSLP) is produced by keratinocytes and plays a central role in the pathogenesis of AD. Whether TSLP is directly responsible for the severe itching associated with AD is unclear.

**STUDY POPULATION.** Studies were performed with mice and human cells.

**METHODS.** TSLP-mediated neuronal signaling was assessed by using calcium imaging and electrophysiology. TSLP-inducing signaling pathways were studied in human primary epithelial cells.

**RESULTS.** The authors observed that direct injection of TSLP into the skin of mice resulted in itching behavior. TSLP-induced itching occurred in mice genetically deficient for lymphocytes or mast cells, suggesting that the pruritic properties of TSLP were independent of its effects on the immune system. Interestingly, dorsal root ganglia from humans and mice were found to express the TSLP receptor, indicating that neurons may be biologically responsive to TSLP. Indeed, treatment of nerve cells with TSLP resulted in calcium influx in a subset of cells expressing the irritant receptor TRPA1, demonstrating that TSLP could act directly on the nervous system. Finally, the authors found that TSLP induction in keratinocytes was dependent on nuclear translocation of the nuclear factor of activated T cells transcription factor, which could be suppressed by the calcineurin inhibitor cyclosporine.
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