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.

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**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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