IgE-Specific Immunoadsorption for Treatment of Recalcitrant Atopic Dermatitis

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Report of Cases
Two consecutively recruited patients with atopic dermatitis (AD) (a man in his 50s [patient 1] and a man in his 40s [patient 2]) displayed high serum IgE levels of 40,848 and 111,696 μg/L (to convert to milligrams per liter, multiply by 0.001), Scoring Atopic Dermatitis (SCORAD) scores of 66 and 77, respectively, and a history of no substantial or long-term SCORAD reduction after use of topical corticosteroids and calcineurin inhibitors, UV light therapy, systemic corticosteroids, and cyclosporine A.

Therapeutic Challenge
We investigated, for the first time to our knowledge, the clinical efficacy and safety of a recently developed IgE-specific immunoadsorption (IA) therapy in these 2 patients.

Solution
Written informed consent was obtained from patients before participation in this treatment protocol. This investigation was approved by the ethics committee of the University of Lübeck and followed the Declaration of Helsinki. As in our previous study using immunoglobulin isotype-nonspecific IA for patients with AD, 12 cycles of 5 IA sessions on days 1 to 5 (week 1) and days 29 to 33 (week 5) were performed. In each IA session, plasma was separated using a blood cell separation technique (Life-18 Apheresis Unit; Miltenyi Biotec) followed by alternate application of 2 patient plasma volumes to 2 adsorption columns (30-35 cycles of approximately 8000 mL separated plasma) containing monoclonal mouse anti–human IgE (TheraSorb-IgE; Miltenyi Biotec). In patient 1, central venous access was required, and in patient 2, a peripheral venous catheter was used. Use of previously prescribed medications consisting of topical class III corticosteroids and calcineurin inhibitors (both patients), as well as cyclosporine A and oral antihistamines (patient 2), was initially continued without change of frequency and/or dosage and later reduced in accordance with disease activity. Reduction or discontinuation of cyclosporine A therapy was not included in the study protocol to avoid a possible relapse, which would have interfered with evaluation of clinical outcome parameters.

Patient 1 showed a satisfactory result (SCORAD reduction by up to 48% to a score of 34 at week 17), and a good response was observed in patient 2 (SCORAD reduction by up to 65% to a score of 27 at week 25). The mean SCORAD improved by 33%, 37%, 54%, 53%, 55%, and 49% at weeks 3, 5, 9, 13, 17, and 25, respectively (Figure). Reduction of long-term topical corticosteroid and calcineurin inhibitor consumption was achieved in patient 2. Treatment was well tolerated.

The mean reduction in circulating IgE for each IA cycle was 92%, with nadirs of 3456 and 7200 μg/L in patients 1 and 2, respectively. Less substantial reductions in IgM, IgG, and IgA were observed, with means of 49%, 37%, and 36%, respectively. All immunoglobulin levels dropped abruptly following IA sessions and then started to increase again approximately 12 hours later, reaching concentrations similar to baseline within 3 weeks.

Discussion
There is overall increasing evidence derived from case series indicating that patients with AD may benefit from anti-IgE treatment with omalizumab. In contrast, 2 randomized clinical trials showed no significant difference in clinical outcomes between patients with...
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REFERENCES


AD receiving omalizumab and those receiving placebo, although only a limited number of patients were investigated and some clinical improvement was noted during anti-IgE therapy.3,4 In addition, some case reports described lack of efficacy of omalizumab in patients with AD.5,6 It has been proposed that this treatment is more likely to be efficacious in the subgroup of patients with AD who (1) do not present with extremely high pretreatment IgE levels considerably exceeding the threshold for Food and Drug Administration-recommended omalizumab dosing (ie, 1680 μg/L for weight ≤60 kg),5,6 (2) have acute rather than chronic forms of disease,3 and (3) lack filaggrin mutations and display higher serum levels of phosphatidylcholines.6

We recently confirmed previous observations of a positive response to anti-IgE treatment in AD using immunoglobulin isotype-nonspecific IA as an alternative IgE depletion method in 10 patients with treatment-refractory AD and excessively high serum IgE levels.7 Our present investigation revealed similar beneficial early and continuous effects of IA on SCORAD compared with our preceding study,ie, mean improvement by 33% and 38% at week 3 and by 53% and 59% at week 13, respectively. The more extended observation period of up to 6 months in the present study (vs 3 months in our previous study) suggests that IA treatment may have long-term clinical efficacy. However, near the end of the observation period, patient 1 experienced a slight increase in SCORAD (from 34 at week 17 to 44 at week 25—still lower than before initiation of IA) and we were not able to reduce his concomitant AD treatments.

Whereas each IA cycle serum IgE levels were specifically reduced by a mean of more than 90%, the concomitantly observed decrease of the other immunoglobulin isotypes, albeit to a considerably lower and clinically nonrelevant degree (eg, serum IgG levels remained within the reference range), may likely be attributed to common unspecific protein loss during elution processes of adsorber columns using column-rinsing buffer and IA-related dilution procedures (eg, use of anticoagulant solution) as reported earlier.7,8 In contrast, IA cycles performed with the immunoglobulin-nonspecific adsorber columns in our previous study lowered serum levels of each immunoglobulin isotype by a mean of more than 90%.1 Similar to our earlier study, the abrupt decrease and subsequent rapid rebound of serum IgE levels following IA differed from the relatively delayed and prolonged decrease of the SCORAD. This effect could possibly be explained by redistribution of this immunoglobulin from the interstitial space, ie, tissue-bound IgE at inflammatory skin sites, into the intravascular compartment. In fact, a continuous reduction of the amount of skin-bound IgE was observed after IA in our previous study. We hypothesized that this reduction may induce impairment of IgE-mediated antigen presentation, which could explain the decreased skin infiltration by inflammatory cells and normalization of altered epidermal morphology (a process that may be more protracted compared with the observed immediate serological changes) in our former IA-treated study patients.7 Therefore, although skin biopsies were not performed in the present study, we believe that a similar decrease of skin-bound IgE rather than circulating IgE was reflected in the gradual but long-lasting skin improvement using IgE-specific IA.

An advantage of IgE IA over omalizumab therapy in AD may be the greater benefit in patients with extremely high serum IgE levels, which are often present in severe cases (as shown in our present and previous IA studies), thereby overcoming possible treatment challenges associated with insufficient dosing of omalizumab and neutralization of a substantial fraction of serum IgE. It remains to be evaluated whether IA of IgE is more potent in reducing the amount of IgE at the site of inflammation (ie, epidermal-bound or dermal-bound IgE) than omalizumab therapy, for which this treatment effect has also been described.3 Another benefit of IA appears to be its good tolerability, although it has to be stressed that patients with AD requiring a central venous line for IA may be at increased risk for developing Staphylococcus aureus bacteremia, which was observed in a single patient from our previous study.1

Together, this is the first report of the clinical use of IgE-specific IA in general, as well as its specific application for recalcitrant AD associated with high serum IgE levels.