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Article in *Journal of Allergy and Clinical Immunology* · February 2011

DOI: 10.1016/j.jaci.2010.12.115

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86 Basophil Responses in Children Undergoing Immunotherapy for Milk Allergy

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RATIONALE: Basophils reportedly manifest reduced activation during immunotherapy (IT) for food allergy (FA). However, the effect of IT for FA on basophil histamine release (HR) and syk expression, as well as how these parameters relate to clinical outcomes, has not been previously investigated.

METHODS: Spontaneous and stimulated HR was measured from basophil-enriched suspensions from milk-allergic children undergoing sublingual (SLIT) or oral (OIT) IT at baseline (T1), following initial dose escalation (T2), end of build-up (T3) and maintenance (T4). Spontaneous expression of CD63, CD203c, and syk were determined using flow cytometry.

RESULTS: 18/24 subjects demonstrated high spontaneous HR (SHR; median 28%; range 11-79%) at T1. SHR decreased in the OIT but not SLIT group by T3 ($p<0.01$) and remained lower at T4 ($p=0.01$). HR to milk, peanut, anti-IgE and f-Met did not change in either group at any time. No change in basophil syk or spontaneous CD63 expression was observed. Spontaneous expression of CD203c increased at T2 ($p<0.01$) in both groups. SHR increased at T2 and T4 in SLIT subjects with relatively worse clinical outcomes, but this distinction was not evident with OIT. However, spontaneous expression of CD63 and CD203c were higher in OIT subjects with worse outcomes at T2 ($p<0.01$ for both markers) compared to baseline, and compared to OIT subjects who did better clinically (CD63 $p<0.01$; CD203c $p=0.05$).

CONCLUSIONS: OIT diminished SHR but failed to reduce intrinsic basophil reactivity to allergen (milk-induced HR or syk expression) despite convincing clinical improvement. Spontaneous expression of CD63 and CD203c during dose escalation may predict clinical outcome.

87 Early and Persistent Gastrointestinal Side Effects Predict Withdrawal from Peanut Oral Immunotherapy (OIT)

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RATIONALE: In OIT trials reported to date, approximately 15-20% of subjects withdrew due to unacceptable side effects; however, little is known about the factors contributing to withdrawal. The objective of this study was to better define these treatment failures.

METHODS: We conducted a review of our ongoing open-label trial of peanut OIT. Demographic, clinical, and immunologic information was abstracted for all enrolled subjects. We compared these variables in subjects withdrawing from OIT at any time, including during the first day desensitization, and those continuing.

RESULTS: Baseline demographics and immunologic parameters were similar between groups. After a median of 37 days (range 1-393), 10/44 subjects (23%) withdrew from the trial at a median dose of 37.5 mg (range 3-2666 mg) due to side effects; one was successfully restarted, leaving nine of 44 as failures (20%). The withdrawal group consisted of 6 males and 4 females with a median age of 55.5 months. Persistent abdominal pain and/or vomiting prior to the 100 mg dose occurred in seven of 10 (70%) of the withdrawal group, compared to 6 of 28 (21%) of those continuing [$p=0.003$; RR 5.6 (95%CI 1.70-18.25)]. Abdominal symptoms quickly resolved upon discontinuing OIT in all but one subject, whose persistent symptoms led to esophagogastroduodenoscopy and the diagnosis of eosinophilic esophagitis.

CONCLUSIONS: Subjects unable to tolerate peanut OIT tend to have early and persistent abdominal symptoms rather than anaphylaxis. Further study is needed to understand the mechanism of these side effects and their long term sequelae.

Funding: NIH-NIAID 1R01-AI068074; Dorothy and Frank Robins Family Fund

88 Treatment Of Severe And Persistent Food Allergy With Omalizumab

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RATIONALE: Severe food allergy is a life threatening condition with few therapeutics alternatives. A pilot study with Omalizumab, as an alternative treatment in persistent milk and egg allergy, has been conducted.

METHODS: Children above 6 years with IgE-mediated allergy to milk or egg. Anaphylaxis history and positive skin prick tests (SPT) and sIgE levels against food. Informed consent was required.

Patients received a sixteenth week treatment with anti IgE Ommalizumab. SPT and single blind food challenges (SBFC) were performed after the treatment. Adverse reactions were registered

RESULTS: Seven patients were included, 3 patients suffered allergy to milk and 4 to egg. 5 patients had a positive SBFC at baseline and 2 patients had a previous history of food transgressions with reactions in the last six months.

All patients received antiIgE treatment without any adverse reaction. 6 patients underwent to SBFC and complete tolerance was confirmed in four patients. Two patients presented a positive SBFC, in both cases a higher dose threshold than baseline SBFC were obtained. One patient rejected SBFC. Three patients with persistent allergy were allocated in a specific oral tolerance induction (SOTI) with anti IgE treatment

CONCLUSIONS: Anti-IgE therapy has proven an effective and safe measure in the treatment of the persistent and severe allergy to milk and egg, whether used as monotherapy or as an adjuvant measure to the process of desensitization to food, making it safer and faster procedure.

89 Oral Immunotherapy in a Murine Model of Food Allergy Induces Desensitization with High Dose Antigen and Heated or Native Antigen

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RATIONALE: We developed a murine model of oral immunotherapy (OIT) to test new approaches that would improve efficacy and safety. We tested if low dose antigen, which may favor regulatory T-cells, would provide clinical protection against anaphylaxis. We also tested if heated antigen, which does not trigger anaphylaxis in sensitized mice, could lead to clinical protection similar to native antigen.

METHODS: C3H/HeJ mice were orally sensitized to ovalbumin (OVA) or ovomucoid (OVM) using cholera toxin as adjuvant. For dose studies, mice were given either low-dose (1 mg) or high-dose (increasing up to 50 mg) egg white OIT daily for two weeks and then orally challenged with OVA. For heated antigen studies, mice were given increasing amounts of heated or native high-dose OVM OIT for two weeks and then orally challenged.

RESULTS: Mice treated with high-dose OIT were protected from anaphylaxis (median temperature 38.1°C versus untreated 31.7°C*), while those treated with low-dose OIT were not (median temperature 31.8°C). A suppression of cytokines (IL-13, IL-10, and IFN- γ) was seen with both low and high dose OIT. Heating OVM abolished its ability to trigger anaphylaxis (median temperature 38.5°C versus native 32.8°C*). However, heated OVM OIT still provided protection against anaphylaxis similar to that of native OIT (median temperature heated 39°C and native 38.9°C versus untreated 34.3°C*). (* $p<0.001$).

CONCLUSIONS: Although low-dose OIT was associated with cytokine suppression, it was not sufficient for clinical protection against anaphylaxis. Using heated antigen as OIT was as effective as using native, and could provide a safer alternative to conventional OIT.