

Usefulness of serum interleukin-10 in determining food tolerance

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Key words: double-blind, placebo-controlled food challenge; food allergy; food tolerance; interleukin-10; receiver operating curve.

Food allergy is generally thought to be lifelong, there might be a substantial number of adult patients labelled as having food allergy who have in fact outgrown their allergy (1).

On the other hand, interleukin-10 (IL-10) is a major regulatory cytokine of inflammatory responses which plays a key role in the induction and maintenance of anergic states (2). Moreover, T-cell response to allergens entering the mucosal route is actively suppressed by IL-10 in healthy subjects (3).

The aim of this study was to assess the usefulness of serum IL-10 levels for identifying oral tolerance in patients suffering from hazelnut food allergy as assessed by double-blind, placebo-controlled food challenge (DBPCFC).

This was a prospective study. Patients provided written informed consent and the study was approved by the ethics committees of the participating hospitals. Forty-one adult patients aged 18–60 were selected on the basis of a clear history of hazelnut food allergy and positive skin prick test (SPT) to hazelnut. Double-blind, placebo-controlled food challenge were performed in all patients, based on a previous European multicentre study (4), and were positive in 29 (70.7%) and negative in 12 (29.3%). After DBPCFC to hazelnut, patients were divided into two groups according to the food challenge results (positive or negative). No statistical differences were found

between patients with DBPCFC-positive results and DBPCFC-negative results to the oral food challenges for age, hazelnut allergy symptoms and time of the last hazelnut food allergic reaction (Table 1). However, differences in sex distribution was found between both groups, with a lower number of female patients in the DBPCFC-negative group. No statistical differences were also detected by the parallel line assay for raw hazelnut-SPT performed in both groups.

Hazelnut-specific IgE and IgG₄ were measured (Hytec-specific IgE and IgG₄ enzyme immuno-assay; Hycor Biomedical Inc., Garden Grove, CA, USA). Human serum IL-10 was also measured by enzyme-linked immunosorbent assay (Biolink 2000, Barcelona, Spain). Hazelnut-specific IgE levels did not differ between groups. Regarding hazelnut-specific IgG₄ levels, no statistical significance was found between groups, although high IgG₄ mean values were observed in the hazelnut-tolerant patients. High IL-10 mean values were also found in the DBPCFC-negative group with statistical significance ($P < 0.03$) (Fig. 1).

The receiver operating curve which established the cutoff offering the best sensitivity and specificity for identifying hazelnut tolerance was chosen to study the usefulness of serum IL-10 levels measurement. Serum IL-10 levels 2.28 pg/ml are considered capable of identifying hazelnut tolerance with sen-

sitivity of 82% and specificity of 70% (CI: 68–97%).

Although the DBPCFC is the gold standard for the diagnosis of food allergy, increasingly higher concentrations of food-specific IgE correlate with an increasing likelihood of a clinical reaction and may help to avoid oral food challenges in some cases (5). Interleukin-10 cooperates in the regulatory T-cell response to allergens in healthy subjects, furthermore, high IL-10 levels during and after specific immunotherapy aid tolerance to these allergens (3, 6). Thus, serum IL-10 levels measurement could be useful in the determination of food tolerance in previously food-allergic patients.

In the current study, high IL-10 mean values were found in the DBPCFC-negative group with statistical significance, suggesting a role for this cytokine in the outgrowing of food allergy. Moreover, serum IL-10 levels 2.28 pg/ml are considered capable of identifying hazelnut tolerance with sensitivity of 82% and specificity of 70%, with such sensitivity and specificity, the dosage of IL-10 is nowadays unable to perform as diagnostic or screening test for food tolerance, but the data open room to wider studies in different settings in order to explore the possibility to use it as an additional diagnostic tool in food allergy.

This high IL-10 level obtained in the DBPCFC-negative group suggests a role for this cytokine in outgrowing food allergy, rendering this interleukin a useful

Table 1. Demographic characteristics and allergy history of patients ($n = 41$)

Characteristics	DBPCFC-negative group ($n = 12$)	DBPCFC-positive group ($n = 29$)
Sex (%)		
Male	81	38
Female	19	62
Age (years), mean (range)	33 (19–41)	29 (19–53)
Hazelnut-specific IgE (IU/ml) (mean $\pm$ SD)	4.30 $\pm$ 3.82	4.80 $\pm$ 3.95
Associated pollen allergy (%)	57	64
Hazelnut allergy symptoms (%)		
Local reactions	63.7	62
Systemic reactions (including anaphylaxis)	36.3	38
Time of the last hazelnut food allergic reaction (%)		
< 1 year	43.16	47.78
> 1 year	56.84	52.22

No statistical differences were found between groups for the parameters except sex distribution. DBPCFC, double-blind, placebo-controlled food challenge.

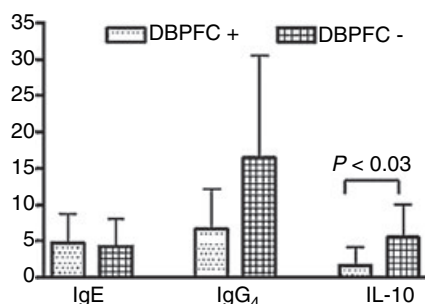


Figure 1. Hazelnut-specific IgE and IgG₄ levels and difference in serum interleukin-10 levels between DBPCFC-positive and DBPCFC-negative groups. DBPCFC, double-blind, placebo-controlled food challenge.

tool in the diagnosis of food tolerance in previously food-allergic patients.

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A visit to the mother in law – a hidden cause for urticaria

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Key word: Urticaria.

Urticaria and angioedema are frequent worldwide, with up to 30% of lifetime prevalence. Especially in spontaneous urticaria forms ('acute or chronic urticaria' according to the GA²LEN/EACCI/EDF guidelines [1,2]) drug intolerance is an important etiological factor.

The guidelines suggest therefore to omit drugs possibly causing urticaria as a first step in the management.

Non-steroidal, anti-inflammatory drugs (NSAIDs) are being the most frequent cause. Aspirin (acetylsalicylic acid) for this reaction the prototype can elicit an episode of wheeling of up to 14 days after a single tablet. Because of the pseudo-allergic nature the onset is sometimes delayed, up to 24 h after the intake, which makes it more difficult for the patient to see the association. Furthermore, in contrast to type I allergic reactions to drugs, neither skin nor *in vitro* tests are available for easy diagnosis.

The present case report illustrates that a pseudo-allergic urticaria reaction to NSAIDs can also be due to hidden and involuntary intake of the drugs.

A 30-year-old male patient came to the Institute of Immunology in Moscow with generalized urticaria. He reported that he had been suffering from repea-

ted episodes during the past months which were getting more intensive every time.

Detailed history revealed neither viral infections nor associated drug intake or a direct correlation to ingested foods. The patient reported no personal history of atopy but after a further investigation it could be revealed that on all occasions he had visited his mother-in-law either on the day or the day before urticaria developed.

The patient was therefore asked to keep a detailed food diary while visiting his mother-in-law. The foods identified in the diary as well as some specimens of home-made food were skin prick tested with negative results in all cases. After further inquiries with his mother-in-law asking for detailed recipes of home-made fruit, it could be revealed that in some of the house-canned fruits, berries and vegetables, the mother-in-law used acetylsalicylic acid as a preservative, which then could be proven as causative agent by a provocation test.

Upon avoidance of aspirin containing home-canned food the patient showed no relapse of urticaria in the following 6 months until writing up this report.

In Russia as well as in some other Eastern European countries it has been an old tradition to prepare home-made canned food of vegetables, fruit and berries for use during the winter period. Not only salt and sugar but also acetic acid are frequently used as preservatives. However, in some of the old cooking books published in the 1950s and 1960s advice was given to use small doses of aspirin (about 100 mg/l) as a preservative since the drug is easily accessible and was very cheap in Eastern Europe at that time (3, 4). Therefore, many of the older people uses this drug for preparing house-canned products until now.

This case not only shows how important good detective work in allergy can be but also how important it is to have a good background knowledge about only seemingly unusual activities in different cultural backgrounds. A note of unexpected occurrence of drugs is therefore suggested to be included in the revision of the EAACI/GA²LEN guidelines for the next consensus meeting in 2008.