

Allergy tests for the diagnosis of culprit allergens in eosinophilic esophagitis: A systematic review.

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To the Editor,

Eosinophilic esophagitis (EoE) is a chronic inflammatory disease with esophageal dysfunction and marked eosinophil-predominant infiltration of the esophagus and a clinicopathologic diagnosis (1,2). Dietary interventions have confirmed the etiological role of food allergens and their combination with topical glucocorticoids is the standard treatment of EoE (1). Three different dietary approaches are usually practiced; an elemental formula diet, “empiric” food eliminations diets (e.g. the 6-FED) and diets based on multimodality allergy testing(1). Skin prick tests (SPT), serum specific (s)IgE, atopy patch tests (APT), but also serum specific (s)IgG4 have been used as allergy diagnostic tools for such diets(1).

Elimination diets can serve as the first step to identify the culprit antigens in EoE; after symptoms’ remission foods can be sequentially reintroduced and food triggers can be defined clinicopathologically (1,2). In the present systematic review, the outcomes of a food-reintroduction diagnostic approach served as comparator to the results of allergy tests serving as diagnostic tools of the EoE food triggers. Our aim was to review the literature on the diagnostic value of allergy tests used in everyday practice.

The detailed methods of the present systematic review are reported in the published protocol (3). The evidence search and selection process are presented in Figure 1. Fourteen studies fulfilling the quality assessment criteria were included in the review; their characteristics are summarized in Table 1 (references in the supplement). The Risk-of-Bias ratings are shown in Table S1. The studies were assessing complete data of 453 EoE patients. Biopsies were used for re-evaluation in all studies, and as the main criterion of EoE remission in most of the studies.

The positive predictive value (PPV) of allergy tests is reported in Table S2. It is deduced by the percentage of allergy tests that have correctly predicted the culprit allergen out of the total number of allergy tests resulting positive. The percentage of patients who responded to treatment was calculated by dividing the number of patients who presented EoE remission after food elimination diets based on positive allergy tests, out of the total number of patients following such diets. Reviewed studies have offered either, or both, of

these data.

Studies have followed a protocol with a single allergy test, or with the combination of two (SPT+sIgE, SPT+APT), or three. Most single-allergy-test studies have reported PPVs lower than 50%. PPV was better for combined tests; PPV of SPT+APT combination was 67.1%, with 65-88.3% of patients presenting symptom amelioration after following a relevant elimination diet. A study combining SPT+APT+sIgE reported symptoms' improvement in 67% of the patients.

The effectiveness of amino-acid-based elemental diet is approximately 90%, while 6-FED shows a 72.1% effectiveness (4). The empiric elimination of cow's milk or dairies is a slightly less-effective strategy. According to our review's outcomes, allergy-test-driven elimination diets have a maximum efficacy of 66-88.3%, so following them is not superior to empirical diets. The decision to follow any of these options, or alternatively a 4-FED or 2-FED, is individualized according to what best fits to patient's lifestyle.

Esophageal prick testing (EPT) performed with food extracts directly on the esophageal lining is a new diagnostic method offering the advantage to examine the local esophageal response to dietary triggers, that might be completely different to IgE-detection with the usual allergy tests (5). Ex vivo food antigen stimulation method, using stimulation of esophageal biopsies with food extracts is another promising alternative (6).

Concluding, although the use of food specific IgE-detection and the performance of APT do not seem useful for selecting which food should be eliminated, it is a fact that personalized elimination of different foods in each patient is highly advised.

Conflict of interest

No author has any conflict of interest to declare.

Authorship Contributors

CP, IT and AC were involved in the conception of the study. Methodology was set by KP, SB and GN. Investigation was performed by KP, who curated the data. Literature citations were imported to Rayyan web application and abstracts were independently checked by CP and EV. ANW was involved a referee. Data were abstracted into a customized data sheet by GPT and MP. Outcomes were validated by KP, SB and GN. CP and EV were involved in original manuscript writing that was reviewed and edited by ANW, IT, AC, SB, CP and GN. All authors approved the final version of the manuscript.

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