Prescriptive appropriateness using inhalant and food allergen panels: a comparison between General Practitioners’ and Allergists’ prescription in Genoa (Italy)

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Summary

Background. Prescriptive appropriateness is an actual claim in healthcare, and it also concerns in vitro tests used in the allergy work-up, such as the serum allergen-specific IgE (sIgE) assay. In the Liguria Region, two panels were defined (for inhaled and food allergens) including 12 allergens. Their composition changed over time. Objectives. The aims of the present retrospective study were: i) to evaluate the percentage of positive tests, and ii) to compare the findings of sIgE assay on the basis of the general practitioners’ (GPs) or specialist’s prescription, considering both the old panels and the new panels. Methods. This retrospective study considered a population of adult patients, which consisted of 2368 subjects (68% females; mean age 50 years; age range: 10-103 years). Serum sIgE were measured by ImmunoCap system.

Results. The percentages of positive tests were very low for food allergens and low for inhaled ones (ranging between 5% to 35%). There was change of prevalent prescriptor with new panels.

Conclusions. This study underlines the relevance of prescriptive appropriateness in the allergy work-up. The sIgE assay should be limited to those allergens that have a clinical relevance, based on clinical history.

Key words

allergen-specific IgE; panels; serum; appropriateness; prescription; specialist; general practitioner

Introduction

Allergic disorders have an impressive prevalence: up to 40% of the general population (1,2). Sensitization is the signature of the impaired immune response to allergen(s) in allergic patients, such as the on-going production of allergen-specific IgE. Sensitization is the condition necessary (but not sufficient) for diagnosing allergy. In fact, allergy is formally documented when symptoms appear after exposure to sensitizing allergen, otherwise sensitization has no clinical relevance. Thus, a sensitization has to be always interpreted during the allergy work up. Sensitization can be demonstrated in vivo (by skin prick test, SPT) or in vitro (by serum allergen-specific-IgE (sIgE) assay): the last is usually more precise, and well-defined serum IgE cut-offs have been associated with likely allergy diagnosis and clinical severity (3,4,5). On the other hand, serum sIgE assay is expensive, and the interpretation needs specific knowledge, mainly concerning molecular components (6,7). In this regard, the convenience of using laboratory resource is extremely timely and indispensable. For a long time, the need of defining the prescriptive appropriateness in laboratory utilization has been acknowledged an impellent requirement. So, a long time ago van Walraven and Naylor performed a systematic review of published studies, that measured inappropriate laboratory use and methodological criteria, including implicit and explicit ones (8). They concluded that many studies confirmed an inappropriate use of laboratory tests. This issue is always more mandatory in light of narrowed healthcare budget and the global concept of appropriateness of care is up-to-date (9). In this context, it is necessary that the prescription of lab test is based on appropriateness criteria. On the basis of this premise, the Italian Health Ministry issued a decree (DM 9 December 2015) that defined the “conditions of dispensation and prescriptive appropriateness indications for a series of health services for outpatients, including tests for al-
Prescriptive appropriateness

Inhaled allergens: the test was performed in 847 patients. The panel was requested more frequently by GPs (96%) than by specialists (4%). Figure 1 reports the percentages of positivity for the single allergens considering the prescription by GPs or specialists. There were significant differences between GPs’ and specialists’ prescriptions, such as positive results were more common for specialists’ prescriptions, for hazelnut tree (p < 0.0001), olive tree (p < 0.0001), *Parietaria officinalis* (p < 0.0001), dog (p < 0.0001), and *Ambrosia trifida* (p = 0.04).

Food allergens: the test was performed in 1187 patients. The panel was requested more frequently by GPs (99%) than by specialists (1%). Figure 2 reports the percentages of positivity for the single allergens considering the prescription by GPs or specialists. There was no significant difference between GPs’ and specialists’ prescriptions for all tested allergens.

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**Materials and methods**

**Patients**

This retrospective study considered a population of adult patients, which consisted of 2368 subjects (68% females; mean age 50 years; age range: 10-103 years). The patients were sent by GPs or specialists to the Laboratory Medicine Service of the University-Hospital San Martino of Genoa (Italy) for serologic assessment, as they suffered from complaints suggestive for respiratory and/or food allergy.

The old panels were in effect from January 2007 to May 2014. The new panels have been introduced in the clinical practice since June 2014.

The old inhaled panel included: *Dermatophagoides pteronyssinus* (D1), *Dermatophagoides farinae* (D2), *Cynodon dactylon* (G2), *Lolium perennis* (M6), birch (T3), hazelnut tree (T4), olive tree (T9), *Parietaria officinalis* (W19), dog (E5), and *Ambrosia trifida* (W3). The old food panel included: egg white (F1), milk (F2), fish (F3), wheat (F4), shrimp (F24), tomato (F25), egg yolk (F75), a-Lactoalbumin (F76), casein (F78), and hazelnut (F17).

The new inhaled panel includes: *Artemisia absinthium* (W5), *Parietaria officinalis* (W19), *Cupressus sempervirens* (T23), olive tree (T9), cat (E1), dog (E5), *Alternaria alternata* (M6), *Dermatophagoides pteronyssinus* (D1), Bet v 1 (T215), Bet v 2 (T216), Pru p 3 (F420), *Phleum pratense* (G6). The new food panel includes: milk (F2), fish (F3), wheat (F4), peanut (F17), soybean (F14), hazelnut (F17), shrimp (F24), egg white (F1), Pru p 1 (F419), Pru p 3 (F420), Pru p 4 (F421), and Bet v 2 (T216).

All patients gave the written informed consent, and the Review Board of the IRCCS-AOU San Martino-IST approved the procedure.

**Assay**

Serum levels of specific IgE were detected by the IFMA procedure (ImmunoCAP, Thermo Fisher Scientific, Uppsala, Sweden) in peripheral blood samples from patients. Serum was collected into gel-separator tubes, centrifuged and stored at -20 °C until analysis. Measurement of circulating specific IgE antibodies was performed according to manufacturer’s instructions (10). Specific IgE concentrations were expressed in kUA/L according to the traceable calibration to the 2nd IRP WHO for Human IgE, and 0.35 kUA/L has been considered as a cut-off for defining positivity, such as sensitization (11).

Analytical quality control was performed both by using an internal quality control (ImmunoCap Specific IgE Control LMH, Thermoscientific, Uppsala, Sweden) and by participating to an external quality assessment scheme (UK NEQAS, Herries Road Sheffield).

**Statistical analysis**

Numbers were analysed by C² test. A p-value < 0.05 was considered as statistically significant. Data were analyzed using Stata statistical package version 13.1 (StataCorp, College Station, TX, USA).

**Results**

**Old panels**

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Figure 1 - New and old panels for inhaled allergens, considering the prescription made by the GP or the specialist.

Figure 2 - New and old panels for food allergens, considering the prescription made by the GP or the specialist.
New panels

Inhaled allergens: the test was performed in 337 patients. The panel was requested more frequently by specialists (62%) than by GPs (38%). Figure 1 reports the percentages of positivity for the single allergens considering the prescription by GPs or specialists. There was significant difference between GPs’ and specialists’ prescription, such as positive results were more common for specialists’ prescriptions, for Pru p 3 (p = 0.0006) alone. Food allergens: the test was performed in 276 patients. The panel was requested more frequently by specialists (60%) compared with GPs (40%). Figure 2 reports the percentages of positivity for the single allergens considering the prescription by GPs or specialists. There was no significant difference between GPs’ and specialists’ prescriptions for all tested allergens.

Discussion

sIgE is usually envisaged as the main biomarker for the allergic phenotype, as allergic disorders are paradigmatically characterized by an IgE-mediated inflammation. IgE measuring is a common way to work up allergy. The present study aimed to investigate the percentage of positive tests and the comparison of the findings considering the GPs’ or specialists’ prescription, both for the old panels and the new panels defined by the Liguria Region. The study was conducted on a large cohort of subjects referring to serologic assessment for suspected respiratory or food allergy. Firstly, this study demonstrated that there was a relevant difference between the number of prescriptions by GPs or specialists: the ratio between GPs’ and specialists’ prescriptions was initially disproportionate in favor of GPs, but then it inverted using the new panels. The percentages of positive tests were very low for food allergens, mainly for old panels, and low for inhaled allergens. These findings denote a scarce appropriateness in using predefined panels. In this regard, it is noteworthy to consider the reimbursement price: € 71.18 for extract allergens (up to 12 allergens) and € 9.92 for each molecular component. On the other hand, the productive cost ranges between € 12 and 15. So the use of panels is in and of itself unprofitable, but considering the present outcomes it seems inappropriate. In fact, an efficacy of 10-30% of panels does not justify their prescription. This consideration agrees with a recent document provided by Italian society of allergy, asthma and clinical immunology (SIAAIC) that reported a list of identified 5 most inappropriate allergological procedures (12). More recently, a document has been published to improve the appropriateness in the field of respiratory allergy suggesting a direct interaction between allergists and policy makers / institutions (13).

Anyway, the current study had some limitations: it was retrospectively conducted on a selected patient population sample, subjects referring for serologic assessment, there was no follow-up, and there are no clinical data. This issue is particularly relevant, as sensitization does not always correspond to allergy: this fact probably further reduces the percentages of subjects really “positive” to tests, such as allergic. In addition, this study did not consider possible confounding factors, such as smoking status, parasite infestation, environmental exposures, seasonal variations, and number of co-sensitizing allergens. Therefore, there is need to conduct cohort studies and long-term follow-up trials to confirm these preliminary findings. However, the strength of the present study is represented by the large size of the sample: higher than in the other studies.

In conclusion, this study underlines the relevance of prescriptive appropriateness in the allergy work-up. The slgE assay should limited to those allergens that are clinically relevant.

References

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