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Review

Utility of Component-resolved diagnosis in allergic disease in children and adults

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Abstract

The component resolved diagnosis is a microarray-based diagnostic solution capable to analyze specific IgE antibodies against 112 allergenic components, providing sensitivity patterns for multi-sensitized or complex patients. The CRD is indicated for these patients, especially those with concomitance of respiratory and food allergy. Here we made a review of the method, his utility, limitations, and our experience in allergic diseases in adults and children with difficult etiologic diagnosis (eosinophilic esophagitis, vernal conjunctivitis, occupational asthma and drug allergy).

Keywords: microarrays, food allergy, occupational asthma, eosinophilic esophagitis, vernal conjunctivitis

Introduction

The introduction of microarray techniques featuring a large panel of purified allergens has been a major advance in the diagnosis of allergic diseases. In summary, those technique, named also component resolved diagnosis (CRD), shows the real sensitization pattern of multi-sensitized patients, helps to difference between cross-reactivity and co-sensitization, helps to rule out allergy, reveals unexpected sensitizations, provide more information in patients with idiopathic anaphylaxis, helps to anticipate the risk and the type of reaction (asymptomatic, local or systemic), guiding decisions about food challenges and helps to identify the IgE profile in patients unresponsive to specific immunotherapy [1-19]. Nevertheless limitations of this tests are also recently described [3-5,13]. In this revision we described the methods of this technique and their applications in the diagnosis of diseases in which an allergic mechanism is still in controversial.

CRD technique

The Immuno Solid-phase Allergen Chip (ISAC®) is a microarray-based diagnostic solution capable of simultaneously analysis of specific IgE antibodies againts 112 allergenic components, providing sensitivity patterns for multi-sensitised or complex patients. The CRD is indicated for these patients, especially those with concomitance of respiratory and food allergy [14].CRD can be useful also in diagnosis of idiopathic anaphylaxis and identification of major sensitization patterns in those multi-sensitised patients.

In up to 9 of every 10 multi-sensitized patients, it has been shown that ImmunoCAP ISAC provides useful and detailed information. CRD can obtain 112 results in each test using a small sample volume (30 microliters). This panel include specific species and molecules related with cross-reactivity.

Thanks to the cross-reactivity components, in addition to 51 allergenic sources, CRD provides information on hundreds of allergenic sources, like food (milk, eggs, fish and shrimp, nut, legumes, wheat, fruits), pollen (from weeds, trees, herbs), animals, moulds, mites and cockroaches, parasites, latex and carbohydrates.

The broad panel of molecular allergens consists of 112 allergenic components fixed in a biochip. A software

generates reports, including orientating remarks in order to aid the interpretation. Only 30 microliters of serum or plasma is necessary. The semi-quantitative results are shown in ISAC standardized units (ISU).

Low background noise provides blank results for the healthy, non-atopic controls, as well as very good specifity for patients with high total IgE, as is the case in patients with atopic dermatitis. The measurement interval, from 0.3 to 100 ISU, providing information on the IgE antibody levels. The ISUs are standardized according to the specific ImmunoCAP units.

The sensitivity varies from 0.3 to 1.0 ISU, depending on the allergenic component. There is no interference, even with a very high total IgE. The allergenic components are deposited in triplets and fixed in a covalent from a polymer-coated microscope slide. Each microscope slide contains 4 microarrays that give results from 4 different samples. The Imnuno CAP develops in two-step assay:

1. The IgE antibodies of the patient's serum are combined with the fixed allergenic components.
2. The IgE antibodies joined to allergens are detected through a fluorescent-marked anti-IgE antibpdy.

The test procedure (including the washing and incubation steps) mean a total assay time of less than 4 hours.

The fluorescence is measured with laser scanner and the results are evaluated using microarray image analysis (MIA) software which in turn generated personalized results reports. In summary, the allergen microarray immunoassay ISAC 112 is a repeatable an reproducible in vitro diagnostic tool for determination of specific IgE [14].

Utility and Limitations

CRD provided information on many allergens, but some important allergens of different sources like tomato, fruits, parasites, drugs, occupational allergens and others are still not included in the microarray commercialized by Thermofisher. The flexibility of the number and types of proteins that can be printed on the microarray allows different set of specific IgE immunoassay analysis to be carried out [9].

Results of some studies indicated that CRD may offer increased specificity, but sensitivity was lacking when compared with standard skin-prick testing and measurement of serum food specific IgE levels [12]. Real-life studies [2,7], show that SPT is less expensive than allergen molecule-based diagnostic testing. However, allergen molecule-based serology was more precise in detecting the disease-causing allergen sources and allowed more precise prescription of immunotherapy which substantially reduced treatment costs and combined costs for diagnosis and treatment. In a study whit 118 patients, a lower number of immunotherapy treatments (n = 119) was needed according to molecular diagnosis as compared to extract-based diagnosis (n = 275), which considerably reduced the total costs for diagnosis and for a 3-year treatment from EUR 1,112.30 to 521.77 per patient.

CRD enables testing for specific IgE against multiple allergens component, more than can be tested by prick, but there are patients that presented diagnostic difficulty. In a "real life" study [7], the ImmunoCAP test should be the preferred single test for possible allergy to nuts, wheat, other specific foods, and anaphylaxis of any cause. In these conditions, SPT and ISAC tests give comparable results. For these authors, the most useful single test for oral allergy syndrome is ISAC, and SPT should be the preferred test for latex allergy [7]. The time process is still too long and the results interpretation depend of qualitative interpretation. There exist the possibility of human errors because is a manual procedure that requires pay a lot of attention.

There also exists the possibility of false negative and positive results using ISAC. This is the special importance in the diagnosis of hymenoptera hypersensitivity. Component-resolved diagnosis based on the use of well-defined, properly characterized and purified natural and recombinant allergens constitutes a new approach in the diagnosis of venom allergy [1]. In recent years, CRD allows for the measurement of IgE antibodies against Api m 1, Ves v 1, Ves v 5, and Pol d 5, as well as cross-reactive carbohydrate determinants (CCDs). These tests are intended to help determine the clinical relevance of any given sensitization, especially in patients with dual sensitization. (Component-resolved tests are a valuable addition to the diagnostic spectrum as long as they are used in combination with established procedures. Apart from Ves v 5, measuring IgE antibodies to Ves v 1 should always be included in the diagnostic workup [6]. Cross-reactive carbohydrate determinants (CCDs) in plants and insect venoms are a common cause of irrelevant positive test results during in vitro allergy diagnosis. Some CCD-positive sera show nonspecific IgE binding even with CCD-free recombinant allergens when using the Phadia ImmunoCAP platform [3]. The diagnostic gap of previously undetected Hymenoptera allergy has been decreased via production of recombinant allergens. Knowledge of analogies in interspecies proteins and cross-reactive carbohydrate determinants is necessary to distinguish relevant from irrelevant sensitizations [4].

Nevertheless the CRD detect more allergens that prick and specific IgE and can be used when these diagnostic tests do not get results. This can be very useful in food allergy and anaphylaxis caused by hidden allergens [10]. A model combining CRD with clinical background and extract-based serology is superior to CRD alone in assessing the risk of severe reactions to hidden allergens in foods, particular in ruling out severe reactions [5, 10]. CRD is useful in the diagnosis of animal allergy [4]. The prevalence of hypersensitivity to marine parasite allergens other than *Anisakis simplex* should be studied, and the most appropriate technique for this is CRD [8].

In pollen allergy the clinical benefit of CRD in

patients sensitized to pollen and fruit related allergens, is very important [13]. The features of the ISAC 112 microarray are similar or superior to those of ImmunoCAP. The CRD is particularly useful for the etiologic diagnosis of pollinosis in patients sensitized to multiple pollen species whose pollination periods overlap [17].

Other important utility of CRD is to control the risk in allergen challenge. Challenge tests for food-dependent exercise-induced anaphylaxis carry risk and have a high rate of false negatives (11). CRD have the potential to provide information of allergen molecules associated with anaphylaxis in order to decide food challenge and to make more accurate assessments of clinical reactivity to food allergens [12].

Allergen molecule-based diagnosis has been suggested to facilitate the prescription of allergen-specific immunotherapy (AIT) [2, 15, 16, 18-23]. The potential role of CRD in circumstances such as the indication of AIT like pollen polysensitization, food allergy, latex allergy or anaphylaxis need a structured approach and more clinical trials [16]. Molecular diagnosis can change allergen-specific immunotherapy prescription in a complex pollen area [18]. In summary and according with the consensus document of the world allergy organization [19], CRD visualize the allergic march and molecular spreading in the preclinical stages of allergic diseases, detecting unknown sensitization, and may indicate that the likelihood of developing symptomatic allergy [15] is associated with specific profiles of sensitization to allergen components. Is also a useful tool in routine allergy diagnostics due to its ability to improve risk assessment, to better select relevant allergens for inmmunotherapy. In this way, the experience of our group in the diagnosis of eosinophilic esophagitis, vernal conjunctivitis, occupational asthma and drug allergy, and the application in an more effective and precise AIT are summarized below

Treatment of Eosinophilic Esophagitis guided by component resolved diagnosis

Eosinophilic esophagitis (EoE) is characterized by esophageal dysfunction and, histologically, by eosinophilic inflammation. There is no etiologic treatment. Component resolved diagnosis (CRD) with microarrays could detect possible allergens involved and indicate an elimination diet and allergen immunotherapy (AIT). No treatment modifies the natural history of EoE and there are no accepted therapeutic targets defining treatment efficacy which, together with the wide heterogeneity of EoE patients, makes common strategies very difficult.

In a study of 67 EoE patients we found CRD-guided diagnosis and allergen immunotherapy (AIT) showed a high percentage of patients were sensitized to environmental allergens, especially pollens, and that after three years CRD-guided diet restriction and AIT, EoE significantly improved [20]. Other recent studies have demonstrated the similarity in AIR response with allergic asthma [21] and the relationship with pollen allergy [22,23] (DELIA) after description of impacted pollinic tubes in esophagus mucosa.

We first hypothesized that, as the esophageal and bronchial mucosa share the same embryonic origin [24], they might respond with similar inflammatory mechanisms to environmental and food allergenic stimuli and that asthma due to allergens and esophagitis may have an equivalent response to AIT.

Some reports suggest that so-called "immunotherapy" with food, (in fact, the induction of tolerance, not to be confused with AIT), is not indicated in EoE. Meta-analyses have been based on very few valid studies. Lucendo et al. [25] selected only three of the 118 reports considered due to their methodology, excluding two good studies in which AIT with aeroallergens improved patients, and concluded that AIT was related to EoE in 2.7% of patients, although the endoscopic study before AIT was not clear. In an EoE patient hypersensitive to a food, the induction of tolerance with the same food could present problems, as may any desensitization technique, albeit controlled.

We also hypothesized that the inflammatory response of the esophageal mucosa in patients with high levels of antibodies to pollen allergens and worsening seasonal EoE may be due to swallowing airborne pollen and the intrusion into the esophageal mucosa of pollen tubes emitted after pollen germination that encounter a pH and humidity resembling the stigma at pollination [26, 27], which might be facilitated by desmoglein deficit [8]. Histological analysis may show callose from pollen and other plant products in the esophageal mucosa.

We aimed to fulfill the classical Koch-Henle postulates [28], which show that a causal agent must be present in each case, must not be found randomly in other diseases or healthy controls, and can be identified in all damaged tissues.

The objectives of this study were: to obtain an accurate etiological diagnosis of EoE using standard allergy tests and CRD; to demonstrate a pathogenic role for environmental allergens in EoE using human and plant histology; and, to evaluate the effectiveness of CRD-guided specific AIT and/or elimination diet.

We made an observational, longitudinal study to compare the effectiveness and safety profile of CRD-guided specific AIT and/or elimination diet with usual EoE maintenance therapy over a 5 year period of real time analysis (real world study). All suitable patients with EoE from two hospitals and 21 primary care centers in the autonomic community of Castile and Leon, Spain, were identified from practice databases and invited to participate in the study. Inclusion criteria were a diagnosis of EoE (symptoms of food impaction and > 15 eosinophils/field on endoscopic biopsy) followed by our Gastroenterology Service from 2010, with a proton pump inhibitor (PPI) trial to confirm the diagnosis and treated for at least nine months with conventional therapy without clinical improvement. 129 patients with EoE were tested

Table 1. Specific allergens detected by CRD, SPT and IgE in > 10% of patients tested.

Positive CRD	Healthy controls n=50	Asthma n=50	Celiac disease n=52	Eosinophilic esophagitis n=129	Total n=282	p (Chi square test)
pol 1	1 (2%)	36 (72%)	13 (24%)	71 (55%)	121 (43%)	<0.001
n Cyn d 1	0 (0.0%)	17 (34%)	8 (15.1%)	50 (38.8%)	75 (26.6%)	<0.001
n Pru p 3	0 (0.0%)	1 (2%)	3 (5.7%)	27 (20.9%)	31 (11%)	<0.001
n Art v 3	0 (0.0%)	2 (4%)	4 (7.5%)	26 (20.2%)	32 (11.6%)	<0.001
r Cor a 8	0(0.0%)	2 (4%)	4 (7.5%)	24 (18.6%)	30 (10.6%)	<0.001
n Jug r1	0(0.0%)	3 (6%)	3 (5.7%)	23 (17.8%)	29 (10.3%)	<0.001
pol 5	0 (0.0%)	6 (12%)	6 (11.3%)	16 (12.4%)	28 (9.9%)	0.08
r Ani s 1	2 (4%)	3 (6%)	0 (0.0%)	15 (12.4%)	21 (7.4%)	0.020
Profilin trees	0(0.0%)	2 (4%)	3 (5.7%)	15 (11.6%)	20 (7.1%)	0..033
Profilin grasses	0(0.0%)	7 (14%)	3 (5.7%)	14 (10.9%)	24 (8.5%)	0.045
Positive SPT						
Lolium perenne (rye grass)	2 (4%)	44(88%)	3(5.7%)	47 (36.4%)	96 (34%)	<0.001
Cynodon dactylon (bermuda grass).	1 (2%)	20 (40%)	3(5.7%)	35 (27.1%)	59 (20.9%)	<0.001
Olea europaea	0(0.0%)	14 (28%)	0(0.0%)	22 (17.1%)	36 (12.8%)	<0.001
Peach	0(0.0%)	3 (6%)	0(0.0%)	16 (12.4%)	19 (6.7%)	0.003
Cuppresus	0(0.0%)	4 (8%)	0(0.0%)	15 (11.6%)	19 (6.7%)	0.006
Hazelnut	0(0.0%)	3 (6%)	0(0.0%)	12 (9.3%)	15 (5.3%)	0.019
Peanut	0(0.0%)	2 (4%)	0(0.0%)	12 (9.3%)	14 (5%)	0.014
Positive IgE						
Lolium perenne	0(0.0%)	25(50%)	4(7.5%)	23 (17.8%)	52 (18.4%)	<0.001
Cynodon dactylon	0(0.0%)	12 (24%)	6(11.3%)	18 (14%)	36 (12.8%)	0.004
Olea europaea	0(0.0%)	6 (12%)	1(1.9%)	16 (12.4%)	23 (8.2%)	0.01
Cupressus spp.	0(0.0%)	1 (2%)	0(0.0%)	11 (8.5%)	52 (18.4%)	0.12
Peach	0(0.0%)	7 (14%)	1(1.9%)	11 (8.5%)	36 (12.8%)	0.15

pol 1: Grass pollen group 1 (includes β-expansins n Lol p 1 from Lolium perenne and r Phl p 1 from Phleum pratense); pol 4,5: Includes r Phl p 5 ribonuclease; n Cyn d 1: Group 1 β-expansin of Cynodon dactylon; n Pru p 3: Peach lipid transfer protein; r Cor a 8: Hazelnut lipid transfer protein; n Art v 3: Mugwort lipid transfer protein; r Jug r1: Walnut 2S Albumin; r Ani s 1: Serin-protease inhibitor of Anisakis simplex; n: native allergen. r: recombinant allergen.

Table 2. Clinical outcomes of EoE patients after two years AIT and/or elimination diet.

Intervention 129 patients with EoE	No AIT/ no avoidance	AIT only	Avoidance only	AIT+ avoidance	Pollen/pollen tubes	Callose
AIT	19	23	19	68	80	76
Group 1 grasses pollen		22		33	55	55
Other pollen mixtures		1		25	25	21
Avoidance						
Hazelnut			1			
Hazelnut+walnut			2			
Peach/fruits			16			
AIT/avoidance						
Hazelnut				23		
rCor a8/hazelnut				22		
Peach/fruits				15		
Sea food				8		
Significant improvement at 2 years	1 (5.2%)	22 (95.6%)	14 (73.7%)	64 (94.1%)	7	3
Symptom free at 2 years	1 (5.2%)	22 (95.6%)	11(57.9%)	64 (94.1%)	6	2

for environmental and food allergens. CRD, histological and botanical analysis was performed. Clinical scores and endoscopic biopsy were performed every six months for 3 years.

Fifty healthy patients, 50 asthmatics due to pollen and 53 celiac disease patients were included as comparison groups. CRD-directed AIT was administered in 91 EoE patients and elimination diet in 140 patients (87 EoE and all 53 CD patients). CRD detected allergen hypersensitivity in 87.6% of patients with EoE. The predominant allergens were grass group 1 (55%), lipid transfer proteins (LTP) of peach and mugwort, hazelnuts and walnuts (Table 1). Callose from pollen tubes was found in 65.6 % of biopsies (Figures 1, 2, 3). After CRD-guided elimination diet and/or AIT, 101 (78.3%) EoE patients showed significant clinical improvement ($p<0.017$) and 97 (75.2%) were discharged (negative biopsy, no symptoms, no medication) without relapse (Table 2). AIT-treated patients had better outcomes (odds ratio 177.3, 95% CI 16.2-1939.0). In conclusion, CRD-directed AIT and/or elimination diet was efficient in treating EoE patients and was well tolerated [21].

Treatment of Vernal Conjunctivitis with Allergen Immunotherapy Guided by Component Resolved Diagnosis

Conjunctivitis is the first symptom of allergic disease in up to 32% of children, mostly associated with rhinitis [1-13]. Vernal Conjunctivitis (VC) is a form of chronic conjunctivitis that mainly affects children living in temperate areas with a strong family history of allergies. It is most common in young males, and usually occurs during spring and summer. The etiology remains unknown and in many cases the prognosis is poor [13].

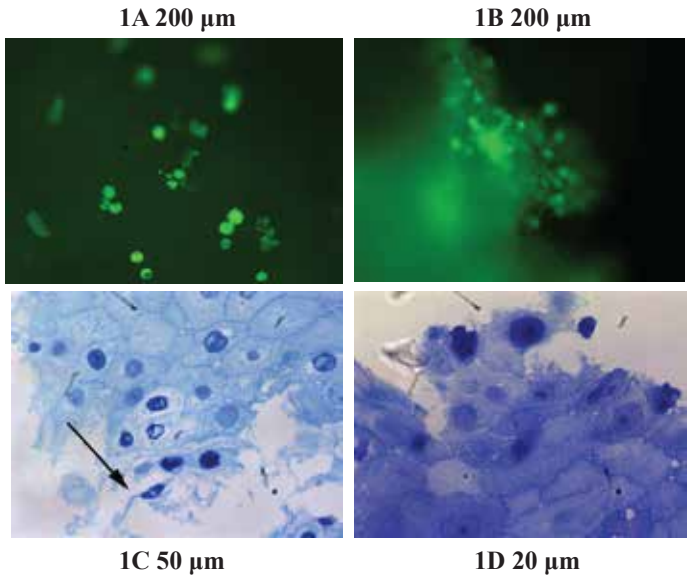
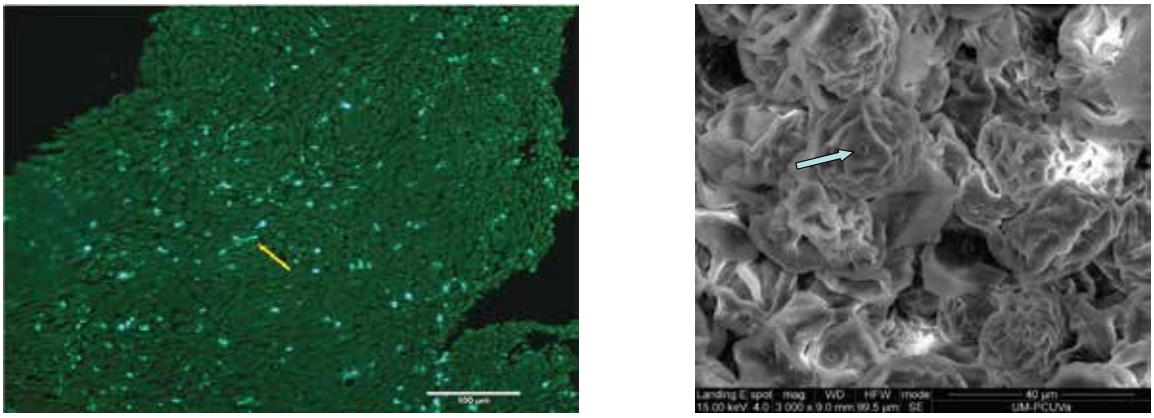


Figure 1. Epifluorescence (A and B) shows pollen, spores and other plant elements on the surface of esophageal biopsies before histological fixation. (C and D): Plant impactions and esophageal mucosae showing damaged epithelial spinous cells. Semi-thin sections with toluidine blue stain. Arrow shows pollen tubes.



(2A) (2B)

Figure 2. A: damaged epithelial cells and intercellular spaces. Arrow shows elongated pollen tube. B: Micro-impaction mainly composed of pollen grains of the Poaceae family infiltrating intercellular spaces. Arrow shows characteristic annulus of grass pollen.

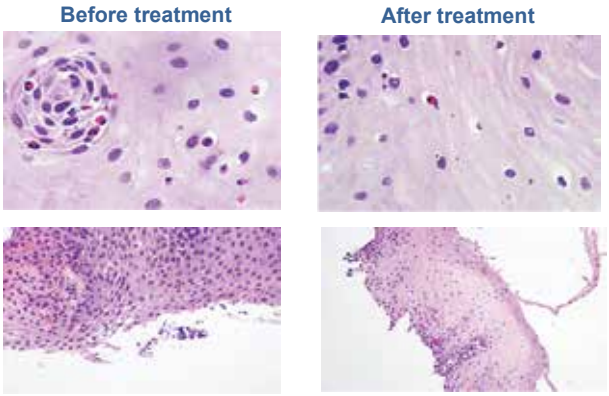


Figure 3. Human histology showed eosinophilic infiltration before AIT and elimination diet with significant decrease of eosinophil infiltrate at two years. EoE biopsies showed eosinophilic infiltration gradually lessened after etiological treatment with diet and specific AIT. (Before AIT H/E 100x, > 15 Eo/CGA: After AIT (H/E 40x). *H/E: Hematosiline-eosine stain.*

Table 3. Component Resolved Diagnosis in Vernal Conjunctivitis.

Positive arrays	Healthy controls n=50	AC n=50	VC n=25	p (Chi square test)
pol 1	1	36	11	<0.001
pol 2	0	34	2	<0.001
pol 4	0	21	3	<0.001
pol 5	0	6	5	0.009
pol 6	0	14	3	<0.001
n Cyn d 1	0	17	9	<0.001
n Der p 1	0	1	2	0.1
n Der p 2	1	1	2	0.31
r Alt a 1	0	2	1	0.36
r Ani s 1	2	3	0	0.46
n Pru p 3	0	1	2	1
r Cor a 8	0	2	2	0.16
n Art v 3	0	2	2	0.16

VC: vernal conjunctivitis; AC: Allergic conjunctivitis; pol 1: Group one of pollen (include the β-expansines n Lol p 1 from Lolium perenne and r Phl p 1 from Phleum pratense); pol 4,5,6: Include r Phl p 5 ribonuclease and r Phl p 6 from Phleum pratense; n Cyn d 1: Group 1 of Cynodon dactylon (Bermuda grass pollen); n Der p 1 and n Der p 2: Cysteine-proteases of Dermathophagoides pteronyssinus and farinae, respectively; r Alt a 1: Acidic glycoprotein of Alternatia alternate; r Ani s 1: Serin-protease inhibitor of Anisakis simplex; n Pru p 3: Peach lipid transfer protein; r Cor a 8: Hazelnut lipid transfer protein; n Art v 3: Mugwort lipid transfer protein.n: native allergen. r: recombinant allergen

Routine diagnostic tests (prick test, specific IgE determination) do not resolve the etiologic diagnosis of VC, and therefore there is no truly specific treatment [6]. Component resolved diagnosis (CRD) uses multiple molecular microarray techniques to improve the diagnosis of allergy-related diseases for which conventional techniques are not efficient [9,14-18].

We have hypothesized that the localization of the hypersensitive response in VC is responsible for the low efficacy of routine diagnostic tests. We have designed a comparative longitudinal study .The aim of this study is to evaluate the IgE-mediated allergic hypersensitivity to aeroallergens by CRD in patients with vernal conjunctivitis, seasonal conjunctivitis and healthy controls.

Twenty-five patients with VC were evaluated. The identified triggering allergens were *n Lol p 1* (11 cases), *n Cyn d 1* (8 cases), group 4 and 6 grasses (6 cases) and group 5 of grasses (5 cases). Prick test and pollen IgE were positive in one case. Clinical improvement was observed in 13/25 VC patients after one-year specific immunotherapy. (Table 3). CRD seems to be a more sensitive diagnostic tool compared with prick test and IgE detection. Specific CRD-led immunotherapy may achieve clinical improvements in VC patients.

Utility of component resolved diagnosis in occupational asthma

Occupational asthma accounts in 10% of all cases of asthma in adults, and baker's asthma is the occupational respiratory disease more prevalent. Occupational asthma accounts for more than 10% of all cases of asthma in adults, and baker's asthma (BA) is the leading cause of occupational respiratory disease in Western countries. Such occupational allergic respiratory disorders are often misdiagnosed, with significant legal, economic, and health impacts for affected patients [1,2].

To avoid specific bronchial challenge with wheat due to its potential risk and technical requirements [4,5]. In recent years, some studies aimed to determine the panel of wheat allergens for diagnosing patients with BA. The

introduction of microarray techniques featuring a large panel of purified allergens has been a major advance in the diagnosis of allergic diseases [6,7]. However this technique has been hardly applied to the diagnosis of patients with occupational asthma caused by wheat [7,8]. In a study, the allergen profiles of patients with BA from 3 different regions in Spain (Madrid, Malaga, and Valladolid) with a relevant bakery industry were characterized. Forty-five bakers with respiratory symptoms (nasal and bronchial) due to occupational exposure to wheat flour, and with confirmed diagnosis of occupational asthma by positive skin prick test (SPT) result and positive bronchial challenge were recruited for CRD study.,

In the t study, more than 80% of these patients recognized some of the printed allergens. The highest prevalence of IgE binding was observed forWTAI-CM16 (54% positivity) and Tri a14 (45% positivity). These allergens were significantly more prevalent in patients with BA than in those from the control groups, covering 64% of the studied population. In contrast, the rest of the purified allergens were recognized by 10% to 30% of the subjects. Receiver operating characteristic curves were calculated comparing SPT and microarray response to Tri a 14 and WTAICM16 as a way to study the validity of the present diagnostic tool.

The wheat allergen profile of our studied BA population was not influenced by environmental allergen patterns. Another fact worth mentioning is that Tri a 14 was recognized only by patients with BA (44%), but not by those who were diagnosed with WFA or SAR.

Utility of CRD in hypersensitivity to illicit drug hypersensitivity

Illicit drugs can cause allergic sensitization in some drug abusers and atopic patients. We have used ImmunoCAP and ISAC in patients with response to cannabis sativa and cocaine, diagnosed after positive bronchial challenges (31). The CRD confirmed positivity to LTPS. These reports suggest that cannabis sensitization may be mediated by 2 mechanisms, cross-reactivity (mainly with LTPs and thaumatin like proteins), and exposure-related de novo sensitisation. LPTS sensitise primarily through the airways. We characterised the molecular sensitisation profile of patients diagnosed with primary cannabis allergy, who experienced asthma after cannabis or cocaine handling or smoking [32,33].

Conclusions

- Molecular analysis or CRD with recombinant and native allergens can be useful in diagnosis of allergy diseases
- The CRD technique was more efficient in the diagnosis of vernal conjunctivitis than skin prick tests and specific IgE.
- Molecular analysis or CRD with recombinant and native allergens can be performed in diseases in which allergic mechanisms are in doubt like eosinophilic esophagitis, occupational asthma and illicit-drug allergy.
- The CRD technique was more efficient in the diagnosis of eosinophilic esophagitis, occupational asthma and illicit drug allergy than skin prick-tests and specific IgE.
- Serum testing with CRD can be a useful tool to guide specific immunotherapy if the antigen cannot be avoided
- Molecular microarray analysis was useful in decision of the treatment, and allowed us to make a more restricted allergen elimination and more precise specific immunotherapy.

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Author contributions

I declare that the authors: Alicia Armentia, Javier Santos, Alfredo Corell and Sara Martín have participated in the conception, design of the study, analysis and interpretation of the data. Blanca Martin carried out all laboratory analyses and Sara Martin and Alfredo Corell the study of celiac patients and patients suffered from vernal conjunctivitis. All authors have participated in the preparation and critical revision of the paper and all authors have seen and approved the final version of the manuscript. I also declare that no authors have any conflict of interest in connection with this paper.

Disclosure

Conflicts of interests: The authors report no conflict of interest.

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