Improved diagnostic clarity in shrimp allergic non-dust-mite sensitized patients

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ABSTRACT

Background: Allergen specific immunoglobulin E (sIgE) levels predictive of shrimp allergy have not been identified, but these may be helpful in identifying patients at risk for shrimp-induced allergic reactions.

Objective: This study sought to identify component resolved diagnostic tests useful for diagnosis of shrimp allergy in patients with or without house-dust mite (HDM) sensitization to the major allergen cysteine protease (Der p 1).

Methods: Patients with positive skin-prick test (SPT) results and/or sIgE values were recruited. Shrimp allergy was classified by oral food challenge (OFC) or by a clear history of anaphylaxis after shrimp ingestion. Patients with shrimp allergy and patients who were tolerant were further classified based on HDM sensitivity (Der p 1 > 0.35 kUA/L). Testing for sIgE to total shrimp, and shrimp and HDM components was performed. The Fisher exact test, Wilcoxon sum rank test, and receiver operating characteristics analyses were used to compare sIgE levels in patients with allergy and patients who were tolerant.

Results: Of 79 patients recruited, 12 patients with shrimp allergy (7 with positive OFC results and 5 with a history of anaphylaxis) and 18 patients who were shrimp tolerant were enrolled. Of the patients not HDM sensitized, sIgE levels to shrimp (10.5 kUA/L, $p = 0.012$) and Der p 10 (4.09 kUA/L, $p = 0.035$) were higher in patients with shrimp allergy. Shrimp sIgE of ≥ 3.55 kUA/L had 100% diagnostic sensitivity and 85.7% specificity (receiver operating characteristic 0.94 [0.81, 1.0] 95% CI) and Der p 10 sIgE levels of ≥ 3.98 kUA/L had a diagnostic sensitivity of 80% and specificity of 100% (receiver operating characteristic 0.86 [0.57, 1.0] 95% CI) for prediction of clinical reactivity.

Conclusion: HDM sensitization influences shrimp and HDM component sIgE levels and, consequently, their diagnostic accuracy in shrimp allergy. In our series, in the patients who were non-HDM sensitized, a shrimp sIgE level of >3.55 kUA/L showed 100% sensitivity and, Der p 10 sIgE of >3.98 kUA/L showed 100% specificity for the diagnosis of shrimp allergy. These levels may not be applicable to every patient and, therefore, may not obviate the need for OFC.

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Shellfish are among the most allergenic classes of seafood.¹ A random telephone survey study reported the prevalence of shellfish and/or fish allergy as 5.9% of households.² The prevalence of U.S. shrimp allergy (SA) was as high as 44–82% of all patients with positive skin-prick testing (SPT) results.³ Clinical history, SPT, specific immunoglobulin E (sIgE), and oral food challenge (OFC) are used to diagnose SA, but each method has flaws. Clinical histories of allergic reactions to shellfish can be confusing because other

allergens (seafood and non-seafood) are often concomitantly consumed with shellfish.¹ Better diagnostic methods are needed.

Commercially available shrimp serologic testing has not previously provided high enough specificity or sensitivity to define hypersensitivity or predict clinical reactivity thresholds. More than 50% of individuals with only a history of SA pass a double-blind, placebo-controlled food challenge.⁴ Likewise, the positive predictive value of shrimp SPT is low and limits its use as a confirmatory clinical test. The National Institute of Allergy and Infectious Disease Guidelines for Food Allergy Diagnosis and Treatment⁶ promote food challenge with double-blind, placebo-controlled food challenge or open OFC as the criterion standard for diagnosis.^{4–6}

The major allergen in shellfish is tropomyosin, which is responsible for molecular and clinical cross-reactivity within the shellfish group (shrimp, crab, and lobster) and other invertebrates, e.g., house-dust mite (HDM) and cockroach.^{7–9} Other shrimp allergens, such as arginine kinase (AK), myosin light

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chain (MLC), sarcoplasmic calcium-binding protein (SCP), troponin C, and, more recently, hemocyanin, have been identified as potentially clinically relevant allergens.^{10–14} As with tropomyosin, these allergens also are cross-reactive with invertebrate proteins.

The use of component-resolved diagnostics (CRD) with purified natural or recombinant allergens has improved diagnostic accuracy in peanut allergy. CRD can help predict the severity of allergic reactions in this case.¹⁵ Shrimp SPT and sIgE have inferior predictive value compared with sIgE to shrimp tropomyosin, but tropomyosin sIgE lacks optimal sensitivity (0.71 [0.30, 0.94]; 95% confidence interval [CI]) and positive predictive value (0.71 [0.30, 0.94]; 95% CI) by using a cutoff level of 0.7 kUA/L for clinical use.¹⁶ Although shrimp sensitization has been reported in individuals with concomitant HDM and cockroach sensitization, neither invertebrate has been reported to play a role in allergic reactions to shrimp. In a recent publication, tropomyosin was reported as playing a minor role in HDM-sensitized SA.¹⁷

The primary aim of this study was to determine the diagnostic accuracy of shrimp-component sIgE testing. To our knowledge, there have been no published reports to date that categorized patients with SA based on HDM sensitization. HDM sensitization may modulate expression of clinical SA, so the secondary aim was to correlate HDM sensitivity with the sensitivity and specificity of shrimp-component sIgE testing.

MATERIALS AND METHODS

Patient Selection

Patients were recruited from the Allergy Clinics, Departments of Pediatric and Internal Medicine, Sections of Immunology, Allergy and Rheumatology, Baylor College of Medicine, between August 2014 and January 2016. Of 151 patients with a SA diagnosis and positive sIgE ≥ 0.35 kUA/L, 79 patients were eligible to be in the study with either (1) physician-diagnosed SA with a positive shrimp SPT result and/or elevated sIgE levels, or (2) avoidance of shrimp due to positive shrimp SPT results and/or elevated sIgE level. A total of 102 patients were eliminated because of the exclusion criteria, which included uncontrolled asthma and an inability to avoid antihistamines. Of the 79 eligible patients, 30 patients were enrolled from this cohort. The study was approved by Baylor College of Medicine Institutional Review Board.

SPT and sIgE Testing and Graded OFC

All the patients underwent four SPTs (Greer Laboratories, Lenoir, N.C.), with shrimp, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, cockroach mix (*Blattella germanica* and *Periplaneta americana*). Prick-to-

prick SPT to cooked (boiled for 10 minutes in water) and raw forms of white Gulf shrimp (*Litopenaeus vannamei*) were also performed. A positive SPT result was defined as a wheal diameter of at least >3 mm larger than the negative control, accompanied by erythema 15 minutes after application.

Serum IgE antibodies to shrimp, HDM, and cockroach allergens (f24, mixture of *Penaeus borealis* and *Penaeus monodon*, *Metapenaeus barbata* and *Metapenaeopsis joyneri*, HDM (d1, Der p), cockroach (i6, Bla g) (Der p 1 [cysteine protease], Der p 10 [tropomyosin], recombinant *Penaeus aztecus* [rPen a 1 tropomyosin], native *Penaeus monodon* [nPen m 2, arginine kinase], rPen m 3 [myosin light chain], rPen m 4 [sarcoplasmic calcium-binding protein], and rPen m 6 [troponin C]) were measured by using ImmunoCAP (Thermo Fisher Scientific Phadia, Portege, MI). A level of ≥ 0.35 kUA/L was considered a positive result.

Twenty-five patients consented for an open graded OFC, and five patients with a history of physician-diagnosed anaphylaxis treated with epinephrine, antihistamines, steroids, and/or albuterol were enrolled. Shrimp were prepared before the challenge by boiling in water for ≥ 10 minutes. Shrimp were given with dose doubling every 15 minutes starting with 2 g until a 32-g dose was reached (a total cumulative dose of 62 g). The challenge was discontinued if an objective sign that involved any of the cutaneous (urticarial and/or angioedema, erythema and/or flushing, itching), upper respiratory (sneezing, nasal congestion, rhinorrhea, cough and/or throat clearing), lower respiratory (wheezing), gastrointestinal (vomiting), and cardiovascular systems (tachycardia and hypotension) was elicited according to guidelines by the work group report on OFC testing.¹⁸

Statistical Analysis

Demographics, sIgE values, and SPT results were analyzed by using the Fisher exact test and Wilcoxon rank sum test. Values > 100 kUA/L were designated as 100.1 kUA/L. Receiver operating characteristic analysis to determine the area under the curve, Spearman correlation, and sensitivity and specificity analyses were performed. A p value of ≤ 0.05 was considered significant. The cutoff values for sIgE were determined by sensitivity and specificity analyses.

RESULTS

Categorization of Patients Based on OFC and HDM sensitivity

Shrimp-graded open OFC to shrimp was performed and clinical characteristics of the patients were recorded (Supplemental Table 1). The historical allergic reaction ranged from <1 to 45 years before presentation, and 10 patients never had previous shrimp inges-

Table 1 SPT results on Shrimp Allergic (SA) and Shrimp Tolerant (ST) patients

SPT	SA	ST	<i>p</i> value, SA vs ST
Shrimp extract, no. (%)	10 (87)	12 (67)	0.419
Shrimp extract, median (25th, 75th) wheal size, mm	8 (5.5, 9.5)	7 (4, 10)	0.782
Raw shrimp, no. (%)	5 (83)*	8 (62)#	0.605
Raw shrimp, median (25th, 75th) wheal size, mm	8.5 (5, 11)	5 (3, 12)	0.509
Cooked shrimp, no. (%)	5 (63)§	5 (33)¶	0.221
Cooked shrimp, median (25th, 75th) wheal size, mm	7 (4.5, 13)	3 (0, 6)	0.029
<i>D. pteronyssinus</i> , no. (%)	9 (75)	14 (78)	0.999
<i>D. pteronyssinus</i> , median (25th, 75th) wheal size, mm	11 (4, 18)	9 (5, 15)	0.626
<i>D. farinae</i> , no. (%)	9 (75)	9 (50)	0.26
<i>D. farinae</i> , median (25th, 75th) wheal size, mm	9.5 (4.5, 15)	5 (1, 14)	0.203
Cockroach, no. (%)	7 (70)	10 (56)	0.689
Cockroach, median (25th, 75th) wheal size, mm	9 (3, 12)	4.5 (3, 9)	0.323

SPT = Skin-prick test; SA = shrimp allergic; ST = shrimp tolerant; *D. farinae* = *Dermatophagoides farinae*; *D. pteronyssinus* = *Dermatophagoides pteronyssinus*.

**n* = 6.

#*n* = 13.

§*n* = 8.

¶*n* = 15.

||*n* = 10.

tion. Eighteen patients had no objective symptoms on OFC and were classified as shrimp tolerant (ST). Seven patients developed objective signs at a median dose of 16 g (range, 2–32 g). Three patients received epinephrine for anaphylaxis. No biphasic allergic reactions were noted. Five patients with a history of physician-diagnosed shrimp anaphylaxis and seven with objective symptoms on OFC were classified as SA. Of the 10 patients who had never had shrimp ingestion, 5 patients were SA and 5 patients were ST. The patients were further subcategorized based on HDM sensitivity, defined as sensitization to major allergen cysteine protease, which is not contained in shrimp (Der p 1 $\geq$ 0.35 kUA/L). SPT to HDM extract was not used a criterion to categorize HDM sensitization because it contains HDM tropomyosin and may result in cross-sensitization with shrimp tropomyosin. There were 7 patients with SA and with HDM sensitization and 5 without, and 11 patients who were ST and with HDM sensitization and 7 without HDM sensitization.

Patient Characteristics

Patient age ranged from 4 to 65 years, with a 5:4 male-to-female ratio, and 73% were <18 years old. Asthma (83% SA, 72% ST), allergic rhinitis (92% SA, 100% ST), eczema (67% SA, 56% ST), and food allergy other than shellfish (50% SA, 50% ST) were present in most patients. The median age of a SA diagnosis was 6 years of age for both SA and ST patients. The presence of urticaria was a distinguishing presenting symptom

by clinical history for more SA than ST patients (*p* = 0.031).

SPT and sIgE of SA and ST Patients

The median wheal diameter to cooked shrimp was larger in the SA group than in the ST group (*p* = 0.0294). SPT positivity was not different between the SA and ST groups when using shrimp extract and raw shrimp. Similarly, the SPTs to Der p, Der f, and cockroach were not different between the SA and ST patients (Table 1). Of note, 17% of the SA group had negative shrimp extract SPT (2 mm wheal/12 mm flare) and raw shrimp (1 mm wheal/6 mm flare), and 38% had negative SPT results to cooked shrimp (3 mm wheal/8 mm flare).

The median sIgE level to shrimp was elevated in the patients with allergy (10.2 kUA/L /L) compared with the patients who were ST (1.25 kUA/L) (*p* = 0.04). Four patients who were ST (4/18 [22%]) and one patient who was allergic (1/12 [8%]) had negative sIgE values (<0.35 kUA/L) to shrimp and other shrimp proteins. The median sIgE values to shrimp and HDM components and to cockroach were not different between the groups (Table 2). There was a higher proportion of patients with allergy with elevated Der p 10 sIgE levels than patients who were ST (*p* = 0.026) and a trend for rPen a 1 sIgE (*p* = 0.058), as shown in Table 2. Only two patients in the SA group had sIgE levels to shrimp and rPen a 1 of >100 kUA/L.

Table 2 Summary of IgE results of patients enrolled

sIgE	SA (n = 12)	ST (n = 18)	p, SA vs ST	SA+HDM (n = 7)*	ST+HDM (n = 11) #	p, SA+HDM vs ST+HDM*#	SA-HDM (n = 5) S	ST-HDM (n = 7)¶	p, SA-HDM vs ST-HDM§
Shrimp, no. (%)	11 (92)	14 (78)	0.622	6 (86)	9 (82)	0.228	5 (100)	5 (71)	0.47
Shrimp, median (25th, 75th), kUA/L	10.2 (3.56, 13.6)	1.25 (0.47, 7.85)	0.042	9.89 (1.12, 100)	2.82 (0.47, 23.6)	0.365	10.5 (3.62, 11.8)	1.06 (<0.1, 3.32)	0.012
rPen a 1, no. (%)	10 (83)	8 (44)	0.058	6 (86)	5 (45)	0.054	4 (80)	3 (43)	0.293
rPen a 1, median (25th, 75th), kUA/L	4.8 (0.91, 8.2)	0.2 (<0.1, 4.15)	0.082	4.41 (0.72, 100)	0.11 (<0.1, 15.28)	0.268	5.1 (1.1, 6.7)	0.27 (<0.1, 0.73)	0.086
rPen m 2, no. (%)	4 (33)	7 (39)	0.999	3 (43)	6 (55)	0.999	1 (20)	1 (14)	0.999
rPen m 2, median (25th, 75th), kUA/L	0.17 (<0.1, 10.8)	0.14 (<0.1, 5.48)	0.570	0.28 (<0.1, 33.4)	0.77 (<0.1, 16.8)	0.544	0.11 (<0.1, 0.2)	0.13 (<0.1, 0.16)	0.801
rPen m 3, no. (%)	3 (25)	3 (17)	0.66	2 (29)	2 (18%)	0.999	1 (20)	1 (14)	0.999
rPen m 3, median (25th, 75th), kUA/L	<0.1 (<0.1, 0.84)	0.06 (<0.1, 0.18)	0.743	<0.1 (<0.1, 1.54)	0.11 (<0.1, 0.21)	0.961	<0.1 (<0.1, <0.1)	<0.1 (<0.1, 0.16)	0.629
rPen m 4, no. (%)	4 (33)	3 (17)	0.392	2 (29)	1 (9)	0.25	2 (40)	2 (29)	0.999
rPen m 4, median (25th, 75th), kUA/L	<0.1 (<0.1, 1.02)	<0.1 (<0.1, 0.12)	0.405	<0.1 (<0.1, 1.17)	<0.1 (<0.1, <0.1)	0.619	0.13 (<0.1, 0.87)	<0.1 (<0.1, 0.65)	0.665
rPen m 6, no. (%)	4 (33)	1 (6)	0.128	3 (43)	1 (9)	0.051	1 (20)	0	0.417
rPen m 6, median (25th, 75th), kUA/L	<0.1 (<0.1, 1.32)	<0.1 (<0.1, <0.1)	0.209	<0.1 (<0.1, 12.9)	<0.1 (<0.1, <0.1)	0.188	<0.1 (<0.1, <0.1)	N/A	0.708
Der p 1, no. (%)	7 (58)	11 (61)	0.999	7 (100)	11 (100)	0.622	0	0	
Der p 1, median (25th, 75th), kUA/L	2.8 (<0.1, 13.99)	2.69 (<0.1, 48.6)	0.615	9.97 (3.6, 28.8)	38.6 (2.81, 70.6)	0.4414	N/A	N/A	
Der p 10, no. (%)	10 (83)	7 (39)	0.026	6 (86)	5 (45)	0.035	4 (80)	2 (29)	0.242
Der p 10, median (25th, 75th), kUA/L	4.0 (1.6, 10.99)	0.2 (<0.1, 6.78)	0.072	3.61 (0.73, 75)	0.26 (<0.1, 17.4)	0.363	4.09 (3.98, 6.97)	<0.1 (<0.1, 0.61)	0.035
Cockroach, no. (%)	11 (92)	11 (65)	0.187	6 (86)	8 (80)	0.228	5 (100)	3 (43)	0.081
Cockroach, median (25th, 75th), kUA/L	4.92 (1.8, 8.1)	1.51 (0.19, 83.16)	0.163	2.27 (0.66, 31.7)	6.48 (0.54, 12.3)	0.961	6.66 (3.66, 6.66)	0.32 (<0.1, 1.76)	0.004

IgE = Immunoglobulin E; sIgE = specific immunoglobulin E; SA = shrimp allergic; ST = shrimp tolerant; HDM = house-dust mite; rPen a 1 = recombinant *Penaeus aztecus* tropomyosin; rPen m 2 = recombinant *Penaeus monodon* arginine kinase; rPen m 3 = recombinant *Penaeus monodon* myosin light chain; rPen m 4 = recombinant *Penaeus monodon* sarcoplasmic calcium binding protein; rPen m 6 = recombinant *Penaeus monodon* troponin C; N/A = not applicable.

*SA+HDM indicates SA and HDM sensitized.

#ST+HDM indicates ST and HDM sensitized.

§SA-HDM indicates SA and non-HDM sensitized.

¶ST-HDM indicates ST and non-HDM sensitized.

||The percentage represents IgE $\geq$ 0.35 kUA/L.

Bold values are p values < 0.05.

Table 3 Sensitivity, specificity, ROC, and AUC for shrimp, rPen a 1, and Der p 10 IgE levels

	SA vs ST	SA vs ST in HDM Sensitized	SA vs ST in HDM Nonsensitized
Shrimp IgE cutoff, kUA/L	3.55	7.85	3.55
Sensitivity, % (95% CI)	83.3 (51.6, 97.9)	57.1 (18.4, 90.1)	100 (47.8, 100)
Specificity, % (95% CI)	66.7 (41, 86.7)	54.5 (23.4, 83.3)	85.7 (42.1, 99.6)
ROC AUC (95% CI)	0.72 (0.53–0.92)	0.63 (0.34–0.92)	0.94 (0.81–1.0)
rPen a 1 cutoff, kUA/L	2.48	4.41	1.1
Sensitivity, % (95% CI)	66.7 (34.9, 90.1)	57.1 (18.4, 90.1)	80 (28.4, 99.5)
Specificity, % (95% CI)	72.2 (46.5, 90.3)	63.6 (30.8, 89.1)	85.7 (42.1, 99.6)
ROC AUC (95% CI)	0.69 (0.49–0.89)	0.66 (0.38–0.93)	0.80 (0.47–1.0)
Der p 10 cutoff, kUA/L	2.43	3.61	3.98
Sensitivity, % (95% CI)	75 (42.8, 94.5)	57.1 (18.4, 90.1)	80 (28.4, 99.5)
Specificity, % (95% CI)	72.2 (46.5, 90.3)	54.5 (23.4, 83.3)	100 (59, 100)
ROC AUC (95% CI)	0.69 (0.49–0.90)	0.63 (0.35–0.91)	0.86 (0.57–1.0)

ROC = Receiver operating characteristic; AUC = area under the curve; rPen a 1 = recombinant *Penaeus aztecus tropomyosin*; IgE = immunoglobulin E; SA = shrimp allergic; HDM = house-dust mite; ST = shrimp tolerant; CI = confidence interval.

Shrimp sIgE Levels of Patients with SA and Patients with ST Based on HDM Sensitivity

In patients without HDM sensitization, median shrimp sIgE levels ($p = 0.012$), Der p 10 sIgE levels ($p = 0.035$), and cockroach sIgE levels ($p = 0.004$) were significantly higher in SA than ST patients, whereas sIgE levels to rPen m 2, rPen m 3, and rPen m 4 were not different between the two groups (Table 2). When sIgE was analyzed to compare patients who were HDM sensitized and SA or ST (Der p 1 ≥ 0.35 kUA/L), there was a trend toward higher median levels of shrimp, rPen a 1, and Der p 10 sIgE in the SA versus the ST group. Because shrimp sIgE levels were higher in the patients with SA than in patients with ST, the cutoff value to predict clinical reactivity was determined (Table 3). The sensitivity and specificity at 95% CI were highest for SA patients with non-HDM. A shrimp sIgE cutoff level of 3.55 kUA/L had an area under the curve of 0.94 (0.81, 1.0, 95% CI), sensitivity of 100%, whereas the specificity of Der p 10 at a sIgE cutoff value of 3.98 kUA/L was 100%. Therefore, these two component tests (rPen a 1 and Der p 10 sIgE) could be used to determine a SA diagnosis in patients without HDM sensitization, with 100% sensitivity and 100% specificity.

DISCUSSION

Shrimp is one of the less studied food allergens compared with peanut, cow's milk, and egg, and, yet, it is also one of the most common foods implicated in emergency department food-allergy visits.¹⁹ In fact, the previously reported rate of anaphylaxis to shrimp is 12% in children and 42% in SA adults with.^{20,21} Currently, OFC remains the criterion standard for the diagnosis of food allergy but OFCs to shrimp are less reported in

the literature than OFCs to other foods. Hence, less-invasive tools are needed to aid clinicians in the diagnosis of shrimp allergy. For patients not sensitized to HDM, the component tests for rPen a 1 and Der p 10 could improve the diagnostic clarity for shrimp allergy in clinical situations when the diagnosis is uncertain.

Shrimp is one of the most common food allergens, and clinicians still face a challenge in interpreting SPT and sIgE results due to a lack of well-established predictive values that correlate with clinical reactivity. A main limitation is the presence of cross-reacting proteins in shrimp and nonedible arthropods, which are common causes of environmental allergies. Shrimp sensitization has been shown to correlate with HDM and cockroach sensitization but may not necessarily relate with clinical reactivity on shrimp ingestion.^{22–25} SPT to commercial shrimp extract has a low diagnostic efficiency (50.6–65.7%).^{16,26} Our findings showed that SPT results with commercial shrimp extract and raw shrimp were not accurate. However, a cooked shrimp SPT results with a wheal size of ≥ 7 mm may aid in screening patients suspected of SA. Cutoff values for SPT wheal size to peanut, egg, sesame, and cow's milk have been reported but not for shrimp.^{27,28} To our knowledge, this is the first study to demonstrate the utility in the diagnosis of shrimp allergy when using cooked rather than raw shrimp SPT wheal size.

Currently, only shrimp sIgE is available for use clinically, and this test alone for a diagnosis of shrimp allergy is not reliable because of cross-reactivity among arthropod proteins. Recent reports show that sIgE values, like SPT, has low diagnostic efficiency (56.9–74.2%).^{16,29} Herein, we showed that SA patients have higher median shrimp sIgE values than ST patients but with modest sensitivity and specificity. We showed

that a shrimp sIgE cutoff level of 3.55 kUA/L had more value in patients without HDM sensitization, likely due to the absence of immunologic cross-reactivity of HDM proteins with shrimp proteins in these patients.

There are published reports of improving the diagnosis of shrimp allergy through molecular diagnosis and CRDs. IgE epitope recognition to individual shrimp allergens in individuals with challenge-proven shrimp allergy provided modest diagnostic efficiency (Lit v 1 epitopes 2, 5a and 5b: 80.8%; Lit v 2 epitope 6: 84.6%),⁴ whereas only a combination of IgE epitope recognition to tropomyosin and SCP has been associated with clinical reactivity.¹⁴ Shrimp epitope recognition may also be a useful tool in the future to predict the natural history of shrimp allergy. There is greater and more intense epitope recognition of shrimp allergens in children compared with adults.³⁰ Although epitope mapping is sensitive, interpretation of results may be difficult because IgE and IgG4 binding areas may largely overlap.

Diagnostic efficiency of sIgE to individual shrimp components have been inconsistent, especially for the major allergen tropomyosin.^{16,26,29} However, it should be noted that the methodology used for determining shrimp tropomyosin differs from previous methods of chimeric enzyme-linked immunosorbent assay, fluoroimmunoassay, and/or immunoblotting. This study showed that the ImmunoCAP measurement of sIgE value to whole shrimp, shrimp tropomyosin (rPen a 1) and HDM tropomyosin (Der p 10) may be used to diagnose shrimp allergy in specific populations. However, a larger data set and multicenter study would be needed in the future to confirm findings and potentially apply component testing in clinical practice. In this cohort, the majority of SA patients, regardless of HDM sensitivity, had a greater proportion of total shrimp sIgE binding to shrimp tropomyosin (80–86%), which suggested it was the major relevant shrimp allergen. Also, sIgE to other shrimp proteins, such as AK (nPen m 2), MLC (rPen m 3), SCP (rPen m 4), and troponin C (rPen m 6), was not more prevalent in this cohort of patients with SA when compared with tropomyosin.

There were limitations to this study, including the small number of patients and an open OFC was done, which is not appropriate for adults and older children. In addition, the overall rate of positive OFC results in this cohort of the SA patients was 28%, which was lower compared with previous reports (32–75%).^{4,14,16,26,29} The lower positive shrimp OFC rate in our study may be due to differences in our population because most were children. Also, the results of SPT or sIgE is influenced by multiple factors, such as total IgE, duration and degree of avoidance of the suspected foods, severity of presentation, the provoking dose for each individual patient, and the food allergenicity.

CONCLUSION

The use of shrimp and CRD sIgE was helpful in predicting clinical reactivity in patients with shrimp allergy who were not HDM sensitized. Herein, we provided evidence on the applicability of CRDs in this important but poorly studied food allergy. Homologous proteins in HDM and cockroach limit CRDs use in HDM-sensitized SA. A shrimp sIgE level that was 100% sensitive (≥ 3.55 kUA/L) and a Der p 10 sIgE level that was 100% specific (≥ 3.98 kUA/L) could confirm shrimp allergy diagnosis in SA patients who were not HDM sensitized; rPen a 1 sIgE testing may help identify a subset of patients with a history of reactions to shrimp with moderate sensitivity (80%) and specificity (85.7%). SPT to shrimp extract is not a reliable tool in screening, but cooked shrimp SPT is a better test to diagnose clinical shrimp allergy. Based on the above results, cooked shrimp SPT, shrimp sIgE, and CRD testing can improve diagnostic clarity in shrimp allergic disease.

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