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Shrimp sensitization in house dust mite allergic patients

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Abstract

Shrimp tropomyosin has a similar structure to house dust mite (HDM) tropomyosin. In this research, 232 adult patients with symptoms of persistent allergic rhinitis were randomly selected. In the group, 59% were sensitized to *Dermatophagoides pteronyssinus* and 57.8% to *Dermatophagoides farinae*. In total, 128 (55.2%) patients were sensitized to both HDM species and 143 (61.6%) to at least one. Slightly over a quarter (25.4%) of patients were sensitized to shrimp. Of the 35 shrimp-sensitized patients, the sensitization to Der p 10 and Pen a 1 was found in 11 cases (31.4%). There was a strong correlation between IgE Pen a 1 and IgE Der p 10 concentrations. The results indicate that there are other allergens responsible for a high incidence of shrimp sensitization in HDM-sensitized patients. A high convergence of Der p 10 and Pen a 1 levels may indicate that the determination of just one of the above is reasonable.

Keywords

allergy, cross-reactivity, house dust mite, sensitization, shrimp, tropomyosin

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Background

Allergy to house dust mite (HDM) is the main cause of persistent allergic rhinitis in Poland. It is well known that shrimp tropomyosin has a similar structure to HDM tropomyosin and can cause hypersensitivity. Some researchers suggest that inhalatory allergy to HDM is the primary sensitizing allergen in shrimp-allergic patients.[1]

The largest epidemiological study in Poland to date is Epidemiology of Allergic Diseases in Poland (ECAP), a continuation of Community Respiratory Health Survey II (ECRHS II), in which 22,700 subjects were examined. Of them, 7000 patients were qualified for further diagnosis in the form of skin prick test. Nearly a quarter (23.4%) of patients were found to have positive skin prick tests with *Dermatophagoides pteronyssinus* and 14.5% of the patients had typical symptoms of HDM allergy.[2]

The frequency of allergy to crustaceans depends on the climatic zone and the population and is estimated at 0.5%–2.5% of the general population.[3] Sicherer et al. published results of an epidemiological study conducted in the United States where

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the frequency of shellfish allergy was estimated at 2.2%. Allergy to seafood was much less widespread in children than in adults (0.5% vs 2.5%).[4] In 2014, the frequency of food intolerance in the adult population of Mexico was examined using the survey method. The frequency of shrimp hypersensitivity was estimated at 4%.[5]

The aforementioned studies employed a variety of diagnostic methods. Component-resolved diagnosis (CRD) gives additional insight into patients' sensitization profile. The list of available allergen components is growing, but it is still very limited in the case of allergy to shrimp. There are only three shrimp allergen components available – tropomyosin in singleplex and multiplex method (depending on the method Pen m 1 – ImmunoCAP ISAC and ALEX, Pen a 1 – ImmunoCAP, Pan b 1 – FABER, Lit v 1 – FABER), arginine kinase (Pen m 2 only in ImmunoCAP ISAC) and sarcoplasmic calcium binding protein (Pen m 4 only in ImmunoCAP ISAC).[6]

The aim of this research was to establish the frequency of sensitization to HDM and shrimp in Polish patients with symptoms of persistent allergic rhinitis. We formulated the hypothesis that there is a positive correlation between the concentration of IgE specific to shrimp and HDM, due to high homology between shrimp and HDM tropomyosin.

Materials and methods

In this cohort, 232 patients (137 women and 95 men, aged between 18 and 76 years, mean age = 39.5) with symptoms of persistent allergic rhinitis (with symptoms such as nose obstruction, nasal excretion and lack of smell, present at least 4 days a week and for at least 4 weeks in a year) were randomly selected from the patients of the Ward and Outpatient Clinic of Allergology of the Department and Clinic of Allergology, Clinical Immunology and Internal Medicine of the Collegium Medicum in Bydgoszcz. Patients treated for severe chronic diseases and those using drugs that could affect the analysis were excluded. Permission from the Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University Committee of Bioethics (No. KB 147/2015) was obtained for the study. In addition, all patients gave their written informed consent on the participation in the study.

A detailed allergology history was taken from all patients who were also physically examined. Blood was collected from all patients in order to determine the level of IgE (immunoglobulin E) specific for allergens of *D. pteronyssinus, Dermatophagoides farinae*, as well as shrimp (allergen extract containing *Pandalus borealis, Penaeus monodon, Metapenaeopsis barbata* and *Metapenaeus joyneri*).

After initial evaluation of the frequency of sensitization to shrimp, in selected patients, depending on the availability of blood serum, the level of allergen components – tropomyosin of HDM Der p 10 and tropomyosin of shrimp Pen a 1 – was also measured.

All immunological measurements were performed using the highly sensitive immunofluorescence method (ImmunoCAP; Thermo Fisher Scientific). At the time of immunological assay, no other, apart from Pen a 1, shrimp allergen components were available in the ImmunoCAP singleplex method.

The IgE level of >0.35 kU/L was assessed as increased, consistent with the common practice in scientific research.[7] The statistical analysis was performed using Excel and R software, version 3.5.1. Normality of distributions of variables was tested using the Shapiro–Wilk test. The analysis of the effect of qualitative variables on the dichotomous (two distinct values) variable was performed using the logistic regression method. The comparison of values of quantitative variables in two groups was completed using Student's t test (in the cases where the variable demonstrated a normal distribution in groups) or the Mann–Whitney U test (in the other cases).

The correlation between the quantitative variables was analysed using the Pearson correlation coefficient (if both values demonstrated a normal distribution) or the Spearman coefficient (in other cases). The strength of dependencies was interpreted using the following scheme:

- $|r| \geqslant 0.9$ – very strong correlation;
- $0.7 \leqslant |r| < 0.9$ – strong correlation;
- $0.5 \leqslant |r| < 0.7$ – moderate correlation;
- $0.3 \leqslant |r| < 0.5$ – weak correlation;
- $|r| < 0.3$ – very weak correlation (negligible).

Due to a relatively large population in the study, even in case of a weak correlation, it was possible

Table 1. Characteristics of the study population, including allergy to house dust mites and shrimps.

Attribute	Study group (n = 232)	
Sex	Female	Male
	137	95
Age (mean; min–max)	39.5; 18–76	
	41.5; 18–75	36.4; 18–76
Specific IgE	Number of patients/percentage	
Dermatophagoides pteronyssinus	137/59 (0.35–100; median = 6.1 kU/L)	
	78/56.9 (women)	59/62.1 (men)
Dermatophagoides farinae	134/57.8 (0.35–100; median = 8.7 kU/L)	
	76/55.5 (women)	58/61.1 (men)
Shrimp	59/25.4 (0–100; median = 1.59 kU/L)	
	29/21.2 (women)	30/31.6 (men)

to achieve statistically significant results with the Spearman correlation coefficient.

The analysis assumed the significance level of 0.05. Therefore, all *P* values below 0.05 were interpreted as indicating the presence of significant correlations.

Results

In the study population, an increased level of IgE specific for at least one of the analysed HDM species was observed in 146 patients.

Majority of the patients were sensitized to both species of HDM. In general, the frequency of sensitization to *D. pteronyssinus* and *D. farinae* was almost the same (139 vs 138 patients). The characteristics of the study population are given in Table 1.

Among the 232 patients with symptoms of persistent allergic rhinitis, in 59% a sensitization to *D. pteronyssinus* was found and in 57.8% a sensitization to *D. farinae* was found. In the study population, 128 (55.2%) patients were allergic to both HDM species at the same time and 143 (61.6%) were allergic to at least one species.

It is notable that in as much as 25.4% of the patients an increased level of IgE specific for shrimp was found. Co-existence of sensitization to shrimp and HDMs is presented in Figure 1.

Among the 59 patients allergic to shrimp, as many as 39 (66%) demonstrated co-sensitization to both *D. pteronyssinus* and *D. farinae*. Only 8 patients were simultaneously allergic to shrimp as well as one HDM species and 12 were allergic to shrimp with no co-sensitization to HDMs.

The correlation between the levels of IgE specific for shrimp allergens, *D. pteronyssinus* and *D. farinae* was analysed. Considering the fact that the correlated variables demonstrated no normal distribution, the Spearman correlation coefficient was used. A statistically significant ($P < 0.05$) and positive correlation was found between the level of IgE specific for shrimp and those specific for *D. pteronyssinus* and *D. farinae*. However, the strength of correlation turned out to be very weak in that case. Results are presented in Figure 2.

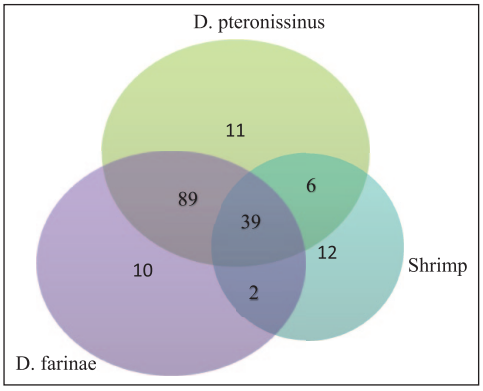
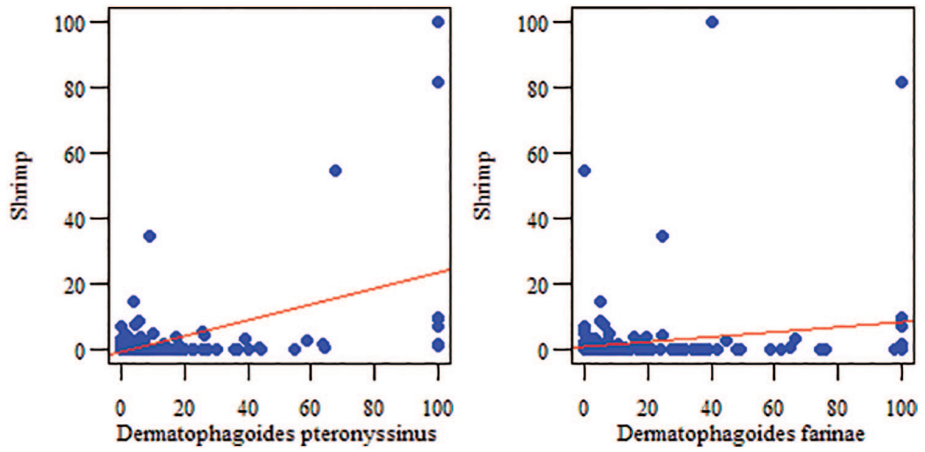


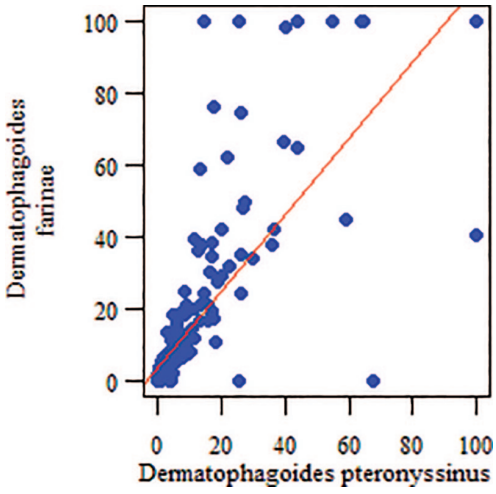
Figure 1. The number of patients allergic to shrimp and simultaneously allergic to house dust mites (number of patients with specific IgE ⩾ 0.35 kU/L).

The correlation between the level of IgE specific to *D. pteronyssinus* and that for *D. farinae* was analysed. Considering the fact that the correlated variables demonstrated no normal distribution, the Spearman correlation coefficient was used. A statistically significant ($P < 0.05$) and positive correlation was found between the levels of IgE specific to *D. pteronyssinus* and *D. farinae*. The strength of correlation was very significant in that case. Results of the analysis are presented in Figure 3.



IgE level (kU/L)	Correlation with the level of IgE for shrimp			
	Correlation coefficient	**p ***	**Direction of a correlation**	**Strength of the correlation**
D. pteronyssinus	0.255	p<0.001	positive	very weak
D. farinae	0.2	p=0.002	positive	very weak

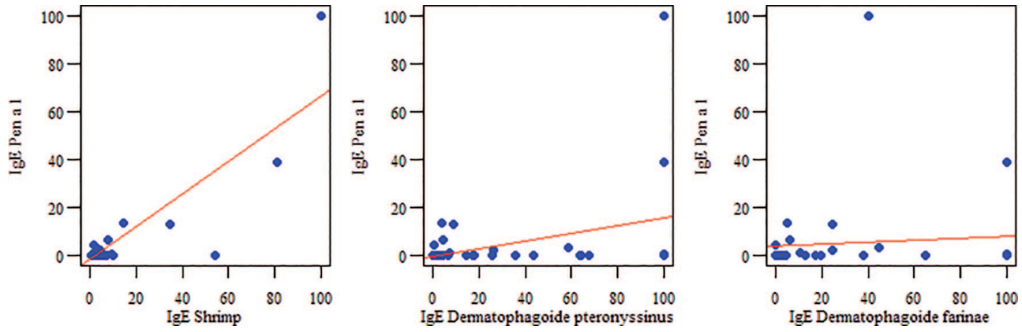
Figure 2. Correlation between the level of IgE specific for shrimp and that for home dust mites.



Analysed attributes	Correlation coefficient *	p	Direction of a correlation	Strength of the correlation
Dermatophagoides pteronyssinus and *Dermatophagoides farinae*	0.92	p<0.001	positive	very strong

Figure 3. The correlation between the level of IgE specific for *Dermatophagoides pteronyssinus* and that for *Dermatophagoides farinae*.

The correlation between the presence of increased (defined as >0.35 kU/L) level of IgE specific to shrimp, *D. pteronyssinus* and *D. farinae* was also assessed. An increased level of IgE specific to shrimp was more commonly associated with the increased IgE level for *D. pteronyssinus* compared to the low level of IgE for *D. pteronyssinus*. The correlation was statistically significant (as $P < 0.05$). An increased level of IgE specific to shrimp was more commonly associated with an increased IgE



Parameter	Correlation with IgE Pen a 1			
	Correlation coefficient	**p ***	**Direction of a correlation**	**Strength of the correlation**
IgE Shrimp	0.672	p<0.001	positive	mean
IgE Dermatophagoides pteronyssinus	0.437	p=0.009	positive	weak
IgE Dermatophagoide farinae	0.445	p=0.007	positive	weak

Figure 4. Correlations between the level of IgE Pen a 1 and IgE *Dermatophagoides pteronyssinus*, IgE *Dermatophagoides farinae* and shrimp.

level for *D. pteronyssinus* compared to the normal IgE level for *D. pteronyssinus*. The correlation was statistically significant (as $P < 0.05$).

In the control group, in all the analysed patients, the level of IgE specific to shrimp, *D. pteronyssinus* and *D. farinae* was below 0.35 kU/L.

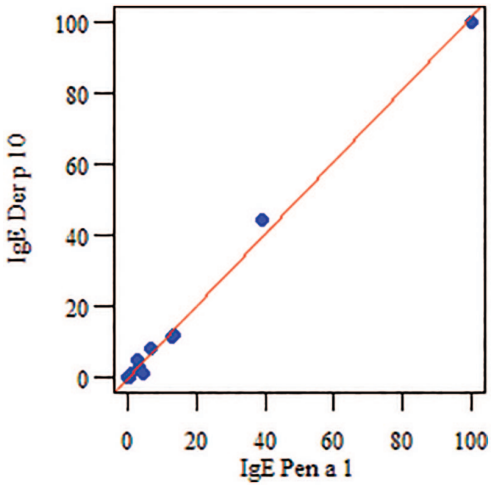
Considering a high incidence of co-sensitization to HDMs and shrimp, a hypothesis was formulated that the reaction was a consequence of an allergy to tropomyosin, the main allergen of shrimp, demonstrating cross-reactivity with tropomyosin of HDMs. In the study population, among the 59 patients who had an increased level of IgE specific to shrimp, the frozen blood serum of 35 patients was still available for testing. In this group, the concentration of IgE specific for tropomyosin from HDMs Der p 10 and tropomyosin from shrimp Pen a 1 was measured. The selection was limited by the amount of blood serum. Among patients with negative history of shrimp allergy and IgE shrimp l < 0.35 kU/L, six were randomly selected into the control group, and IgE Der p 10 and Pen a 1 were determined. All assays were performed using the highly sensitive immunofluorescence method ImmunoCAP.

Among the analysed 35 of 59 patients who had IgE for shrimp level > 0.35 kU/L, the sensitization to tropomyosin, from both HDMs (Der p 10) and shrimp (Pen a 1), was found in just 11 individuals (31.4%). It turned out that the remaining 24 people (68.6%) were probably sensitized to shrimp allergens other than tropomyosin. Correlations between the level of IgE Pen a 1 and IgE *D. pteronyssinus*, IgE *D. farinae* and shrimp were analysed. It turned out that IgE Pen a 1 was significantly and positively correlated with other IgE (as $P < 0.05$), but only in the case of IgE for shrimp the correlation was strong (Figure 4).

The analysis of the correlation between IgE Pen a 1 and IgE Der p 10 levels is very interesting. It turned out that the levels are strongly and positively correlated (as $P < 0.001$), and the correlation was very strong, with a correlation coefficient of 0.987. The correlation is well presented in Figure 5.

Discussion

Allergic rhinitis is a growing problem in Europe. The ECAP study indicated that the incidence of sensitization to HDMs in patients demonstrating



Analysed attributes	Correlation coefficient *	p	Direction of a correlation	Strength of the correlation
IgE Pen a 1 and IgE Der p 10	0.987	p<0.001	positive	very strong

Figure 5. The correlation between IgE Pen a 1 and IgE Der p 10.

symptoms of persistent rhinitis was 61.3%. It was also notable that 55.2% of the patients were allergic simultaneously to *D. pteronyssinus* and *D. farinae*.[2]

Panzner et al.'s study analysed the results of the ImmunoCAP ISAC trial involving 1766 patients from the Czech Republic, who were diagnosed because of suspected allergy. At least one of the following conditions was clinically diagnosed in those patients: chronic rhinitis (73%), bronchial asthma (41%), atopic dermatitis (34%), urticaria or oedema (19%) and/or anaphylaxis (11%). In the study population, allergy to HDMs (Der p 1 or Der p 2) was found in 32.7% of the patients, allergy to shrimp tropomyosin (Der p 10) in 1.9% of the patients and allergy to cockroach tropomyosin in 1.5% of the patients. Overall, allergy to tropomyosin was diagnosed in 2.2% of the study population.[8] In the population of patients with chronic rhinitis, studied by us, the allergy to HDMs was present in 61.6% of the population, which is comparable to the results obtained in the ECAP study and could also be related to the study by Panzner et al. However, a relatively high incidence of sensitization to shrimp allergens is notable in our observations (25.4%). At the same time, we have observed a statistically significant correlation between sensitization to HDMs and shrimp allergens. A hypothesis could be formulated that cross-allergy with tropomyosin could be the cause. Extended diagnostics involved only 35 of 59 patients with an IgE shrimp level >0.35 kU/L, but in that population sensitization to tropomyosin was found only in 11 patients (31.4%). For the remaining 68.4% of the patients, it could be stated that sensitization to shrimp was associated with other proteins, including sarcoplasmic calcium binding protein, or arginine kinase, and sensitization to HDMs was co-existent with sensitization to shrimp.

Boquete et al.[9] indicated that 71% of the patients allergic to HDMs also had IgE specific to shrimp and 55% of them had increased levels of IgE specific to shrimp tropomyosin. In our study population, among the 143 patients allergic to *D. pteronyssinus* or *D. farinae*, an increased level of IgE for shrimp was found in 47 (32.9%) patients. On the other hand, the increased level of IgE for shrimp was present in only 6 out of 89 patients, for whom no increased level of IgE specific for HDMs was found (6.7%).[9] A significant difference between our observations and those of Boquete et al. may result from a relatively lower exposure to shrimp allergens in the Polish population compared to the Spanish one. On the other hand, the study by Boquete et al. was definitely limited by a relatively small population (a total of 70 patients).

Canadian studies demonstrated a high incidence of allergy to HDMs in 95 patients with confirmed allergy to shrimp. In that study population, 86 (90.5%) patients had positive skin prick tests for HDM allergens.[10]

Indications for diagnostics based on allergen components in patients allergic to shrimp and HDMs are the problems that need to be considered. Considering a significant convergence of tropomyosin levels from HDMs (Der p 10) and shrimp (Pen a 1), a question needs to be asked if the measurement of levels of IgE for both species is reasonable, as tropomyosin is a multi-species panallergen. López-Matas et al.[11] demonstrated that the homology between tropomyosin of HDMs belonging to the *Chortoglyphus arcuatus* species and tropomyosins from other allergenic sources was 54%–96%.

On the other hand, Tuano et al.[12] analysed a relatively smaller number of shrimp-allergic versus shrimp-tolerant patients and found 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) in shrimp-allergic patients who were not HDM sensitized. rPen a 1 sIgE testing had moderate sensitivity (80%) and specificity (85.7%).

There are of course several drawbacks to our study. An important limitation is that it has been conducted on a randomly selected population and the inclusion criteria were wide, which makes our group heterogeneous. Due to lack of blood serum remained after the initial immunological assay, only a part of the shrimp-sensitized group had the concentration of IgE Der p 10 and Pen a 1 measured. Also establishing the level of IgE specific to other available shrimp allergen components would add extra value to this study.

To our knowledge, this is the first study on the problem of shrimp allergy in Polish allergic rhinitis patients. Further studies on large populations are necessary to assess what percentage of individuals allergic to Der p 10 could be detected by the determination of Pen a 1.

Author contributions

N.U.-S. contributed to the study design, research material collection and interview with patients; obtained consent and prepared the manuscript. E.G.-U. contributed to the study design and interview with patients and evaluated and corrected the manuscript. K.L. performed the immunoassay. M.Z.-G. performed the immunoassay. Ł.S. evaluated and corrected the manuscript. R.A. evaluated and corrected the manuscript. Z.B. contributed to the study design and evaluated and corrected the manuscript.

Availability of data and materials

The dataset supporting the conclusions of this article is included within the article.

Consent for publication

All authors consented to the publication of the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University Committee of Bioethics (No. KB 147/2015).

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Informed consent

Written informed consent was obtained from all subjects before the study.

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