

Differentiating of cross-reactions in patients with latex allergy with the use of ISAC test

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Abstract

Introduction: Differentiating between cross-reactivity and double sensitization is still a challenging issue in allergology.

Aim: To differentiate cross-reactions accompanying latex allergy with the use of the ISAC test.

Material and methods: Thirty-nine patients reporting immediate allergic reactions to latex were enrolled into the study (group A). The control group was comprised of 41 patients with allergic diseases not associated with latex (group B) and 20 healthy individuals (group C). Their history was recorded and skin prick tests were performed with latex, airborne and food allergens. Specific IgE against food allergens, latex (k82) and recombinant latex allergens were determined. ImmunoCAP ISAC test was performed with 103 molecules.

Results: Sensitization to latex was found by means of skin tests in 16 cases and sIgE against latex was revealed in 12 cases (including 10 positive in both SPT and sIgE). In the ISAC test antibodies against recombinant latex allergens were found in 8 patients with rHev b 6 as the most common. All the patients positive for rHev b 1, 5, 6, 8 had allergy or asymptomatic sensitization to food allergens cross-reacting with latex. Some reactions could not have been differentiated due to the lack of allergens in the ISAC test. Others, not related to latex-fruits syndrome were explained by cross-reactivity with other profilins or PR-10 proteins.

Conclusions: ImmunoCAP ISAC test could be useful in differentiating between cross-reactions and double sensitizations. However, in the case of latex its advantages are limited due to a small panel of allergens.

Key words: latex allergy, cross-reactivity, ISAC test.

Introduction

Prevalence of sensitization to latex is estimated to be about 1%, but only 0.1% of the European population develop immediate reactions after exposure [1, 2]. The risk factors for sensitization include frequent exposure at a workplace (health care facilities, gum industry etc.) and repeated diagnostic or therapeutic medical procedures [3, 4]. Although the first case of anaphylaxis induced by latex was described by Stern in 1927, the problem started to arise when medical gloves were introduced into everyday practice, particularly in the 1980s [5].

Allergy to latex can be manifested either by contact dermatitis (type IV, delayed reaction) or immediate, anaphylactic (type I) reaction, which is more dangerous and may be fatal. Skin, nose and conjunctiva are the most

frequent target organs [6]. In 30–80% of sensitized individuals, cross-reactivity with certain foods is observed, particularly with banana, avocado and papaya (50%), chestnut, kiwi and tomato (30–50%), celery, apple, pineapple and melon (30%) [7–11]. This is due to similarity of epitopes binding specific IgE. Allergens responsible for development of cross-reactions are: Hev b 8 (profilin) – in relation to kiwi, banana, apple, pineapple, tomato, celery; Hev b 11 (class I chitinase) – avocado, banana, chestnut; Hev b 12 (lipid transfer protein) – kiwi, banana, apple, celery, hazelnut, walnut, peach; Hev b 7 (patatin-like protein) – potato.

Diagnosis of latex allergy is usually based on anamnesis, skin prick tests and patch tests, and specific IgE determination. Although very useful in everyday practice, these methods do not make it possible to distinguish

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between double sensitizations and cross-reactions. Understanding of the hypersensitivity mechanism would be useful as it could influence its management.

Aim

The aim of this study was to differentiate cross-reactions accompanying latex allergy with the use of the ISAC test.

Material and methods

Thirty-nine patients reporting immediate allergic reactions to latex were enrolled into the study (group A). The control group was comprised of 41 patients with allergic diseases not associated with latex (group B) and 20 healthy individuals (group C). The patients were recruited in the Department of Allergology, Medical University of Gdansk and healthy controls – among hospital employees. Characteristics of the study population are presented in Table 1.

In all subgroups, exclusion criteria included pregnancy and serious medical conditions which could, in our opinion, affect safety or reliability of planned procedures (current infection, exacerbation of allergic disease, inability to discontinue antihistamines etc.).

In all study participants, their history was recorded including symptoms of latex allergy and other allergic conditions. Skin prick tests were performed with latex and common airborne allergens (Allergopharma, Reinbeck, Germany) as well as food allergens (banana, kiwi, avocado, potato, tomato, celery, carrot, paprika, walnut, hazelnut, peanut, apple) (Stallergenes, Anthony, France) in accordance with EAACI guidelines [12]. Then, blood was collected for determining of specific IgE and the ISAC test. Specific IgE against banana, kiwi, avocado, potato, tomato, celery, carrot, paprika, walnut, hazelnut, peanut, apple, latex and recombinant latex allergens: rHev b 1, rHev b 3,

rHev b 5, rHev b 6.01, rHev b 8, rHev b 9, rHev b 11 were measured by means of ImmunoCAP Phadia System (Phadia, Uppsala, Sweden). ImmunoCAP ISAC test (Phadia, Uppsala, Sweden) was performed with 103 molecules including allergens of latex (rHev b 1, rHev b 3, rHev b 5, rHev b 6, rHev b 8), kiwi (nAct d 1, nAct d 2, nAct d 5, nAct d 8), celery (rApi g 1), carrot (rDau c 1), apple (rMal d 1), peach (rPru p 1, nPru p 3), peanut (nAra h 1, nAra h 2, nAra h 3, nAra h 8), hazelnut (rCor a 1.0401, rCor a 8, nCor a 9), pineapple (nAna c 2) etc. The results were expressed in ISAC standardized units (ISU) as well as in classes: class 0 – < 0.3 ISU; class 1 – 0.3–1.0 ISU; class 2 – 1.0–15.0 ISU; class 3 – > 15 ISU.

All the participants gave written informed consent before the tests. The protocol was approved by the Independent Bioethics Committee of Medical University of Gdansk.

Statistical analysis

In statistical analysis, χ^2 test with Yates' correction was applied for comparison of qualitative variables between the study groups. Value of $p < 0.05$ was considered significant. Software Statistica 8.0 was applied for the calculations (StatSoft, Tulsa, USA).

Results

Thirty-nine patients with a history of latex allergy were enrolled into this study. Most of them reported contact urticaria (38 patients; 97%), rhinitis (8 patients; 20.5%), conjunctivitis (8 patients; 20.5%) and dyspnoea (7 patients; 18%) after exposure. In 3 cases, an anaphylactic shock was documented. Fourteen of these patients reported also reactions to certain food allergens, mostly to banana, kiwi fruit, apple, walnut and hazelnut (Table 2). In group B, food allergy was reported by 16 patients with hazelnut and walnut as the most common allergens.

Table 1. Study population characteristics

Parameter	Group A (n = 39)	Group B (n = 41)	Group C (n = 20)
Age [years]:			
Range	18–68	18–59	21–69
Mean	39.7	32.6	38.7
Gender (women : men)	35 : 4	21 : 20	16 : 4
Concomitant allergic diseases			
Asthma	17 (43.6%)	32 (78%)	–
Rhinitis	24 (61.5%)	36 (87.8%)	–
Conjunctivitis	21 (53.8%)	29 (70.7%)	–
Atopic dermatitis	10 (25.6%)	7 (17.1%)	–
Food allergy	19 (48.7%)	23 (56.1%)	–
Insect venom allergy	7 (17.9%)	5 (12.2%)	–
Drug allergy	14 (35.9%)	16 (39%)	–

Table 2. Prevalence of positive skin prick tests (SPT) and specific IgE (sIgE) to latex (k82) and food allergens in the study groups

Allergen	History		SPT			sIgE		
	Group A	Group B	Group A	Group B	Group C	Group A	Group B	Group C
Latex	39 (100%)	0 (0%)	13 (33.3%)	3 (7.3%)	0 (0%)	7 (17.9%)	5 (12.2%)	0 (0%)
Banana	7 (17.9%)	1 (2.4%)	8 (20.5%)	7 (17.0%)	1 (5.0%)	4 (10.3%)	6 (14.6%)	0 (0%)
Kiwi fruit	8 (20.5%)	3 (7.3%)	10 (25.6%)	6 (14.6%)	0 (0%)	3 (7.7%)	4 (9.8%)	0 (0%)
Avocado	5 (12.8%)	1 (2.4%)	8 (20.5%)	6 (14.6%)	1 (5.0%)	3 (7.7%)	9 (21.2%)	0 (0%)
Potato	3 (7.7%)	2 (4.9%)	7 (17.9%)	8 (19.5%)	2 (10.0%)	2 (5.1%)	7 (17.1%)	0 (0%)
Tomato	2 (5.1%)	4 (9.8%)	8 (20.5%)	6 (14.6%)	1 (5.0%)	3 (7.7%)	7 (17.1%)	0 (0%)
Celery	3 (7.7%)	5 (12.2%)	8 (20.5%)	10 (24.4%)	1 (5.0%)	2 (5.1%)	7 (17.1%)	0 (0%)
Carrot	1 (2.6%)	2 (4.9%)	5 (12.8%)	5 (12.2%)	1 (5.0%)	1 (2.6%)	8 (19.5%)	0 (0%)
Paprika	0 (0%)	2 (4.9%)	7 (17.9%)	7 (17.0%)	3 (15.0%)	1 (2.6%)	5 (12.2%)	0 (0%)
Walnut	6 (15.4%)	7 (17.1%)	9 (23.1%)	4 (9.8%)	2 (10.0%)	0 (0%)	4 (9.8%)	0 (0%)
Peanut	0 (0%)	2 (4.9%)	6 (15.4%)	6 (14.6%)	3 (15.0%)	1 (2.6%)	3 (7.3%)	0 (0%)
Hazelnut	6 (15.4%)	8 (19.5%)	9 (23.1%)	8 (19.5%)	2 (10.0%)	6 (15.4%)	13 (31.7%)	0 (0%)
Apple	7 (17.9%)	4 (9.8%)	1 (2.6%)	2 (4.88%)	0 (0%)	3 (7.7%)	4 (9.8%)	0 (0%)

Histories of food allergy were partly confirmed by skin prick tests. Their sensitivity was between 27% and 63% with relatively high values for celery (63%), banana (50%) and hazelnut (50%). Their specificity was the highest for banana (87%), walnut (87%), and hazelnut (86%). In contrast, no true positive results were obtained for carrot, paprika and apple. The number of positive SPTs was significantly higher in patients with clinical symptoms of latex allergy (group A) compared to patients with other allergic conditions (group B) ($p = 0.0086$). Such differences were not observed in results of sIgE. The sensitivity of their determination was 9–43% and specificity – 88–98%. The highest values were obtained for walnut, kiwi fruit and potato (93–98%).

Sensitization to latex was found by means of SPTs in 13 cases from group A (33.3%) and 3 cases from group B (7.3%). sIgE against latex was revealed in 7 patients from group A (17.9%) and 5 from group B. As far as recombinant allergens are concerned, antibodies against Hev b 6.02 and Hev b 8 were most often found (Table 3). In the ISAC test, antibodies against recombinant latex allergens were found in 8 patients (6 in group A, 2 in group B) with rHev b 6 as the most common (4 patients).

Relations between positive skin prick test (SPT) with latex and food allergy

Out of 16 patients with positive SPTs with latex, 11 reported food allergy (mostly to hazelnut, kiwi, walnut, banana). In 8 participants, the history was confirmed by skin tests and/or sIgE. In the group that did not report any food allergies, 4 were positive in SPT and/or sIgE with

food and only 1 patient was negative in both SPTs and sIgE.

Relations between sIgE to latex and food allergy

sIgE to latex (k82) were positive in 12 patients. Nine of them had a history of food allergy confirmed by SPT and/or sIgE. Three subjects had a negative history, including two positive in SPTs (kiwi and celery). sIgEs against recombinant latex allergens were found by means of ImmunoCAP in 4 patients for Hev b 6.01 (3 with a positive history of food allergy, 4 with positive SPTs and 3 with positive sIgEs), in 5 patients for Hev b 6.02 (4 with a positive history of food allergy, 5 with positive SPTs, 2 with positive sIgEs) and in 5 patients for Hev b 8 (3 with a positive history, 4 with positive SPTs, 5 with positive sIgEs).

Relations between positive latex responses in the ISAC test and food allergy

All the patients positive in the ISAC test for rHev b 1, 5, 6, 8 had food allergy or were asymptotically sensitized. rHev b 5 was positive in one patient who had latex allergy confirmed by SPT and sIgE. Despite no history of food allergy the patient had positive SPTs with kiwi, avocado, potato, tomato, celery, paprika, peanut and hazelnut. The only positive result for rHev b 8 was found in group B. The patient, with chronic asthma, rhinitis and no history of food allergy, was positive in SPT with grass, trees, weeds and walnut, in sIgE – with latex (k82 and rHev b 8), banana, avocado, tomato, celery and carrot, in ISAC – rBet v 2, Phl p 1, 2, 4. Thus, similarity of profilins Bet v 2 and Hev b 8 could explain such reactivity. Four

positive results for rHev b 6 were obtained in patients with latex allergy 3 of whom had food allergy confirmed by SPT and/or IgE (kiwi, hazelnut, walnut, banana, potato) and 1 was found to be asymptotically sensitized to kiwi and hazelnut.

Latex-fruits and pollens-fruits cross-reactions

In patients with confirmed food allergy several patterns of reactivity were found. As far as banana is concerned, allergy was confirmed in 4 patients – one of them was positive in ImmunoCAP for rHev b 8 and rHev b 6.01, another one – for rHev b 6.01, rHev b 6.02, rHev b 11 in ImmunoCAP and rHev b 6 in the ISAC test.

Out of 11 patients reporting hypersensitivity to kiwi fruit, 3 were positive in SPT and/or sIgE, including 2 who were also positive for latex (one for rHev b 6.01 and rHev b 8 in ImmunoCAP and one for rHev b 6.01, rHev b 6.02, rHev b 11 in ImmunoCAP and rHev b 6 in ISAC). In ISAC test four kiwi allergens were included (nAct d 1, 2, 5, 8). We found one positive result for nAct d 1, 2, 8 and none for nAct d 5. Patients positive for nAct 1, 8 tolerated kiwi. The patient with positive result for nAct d 2 reported several pollen and food allergies but the latter were not confirmed either by SPT or ImmunoCAP.

The highest rate of confirmed food allergies was obtained for hazelnut (8/14). Two patients had allergy to pollens and hazelnut with no concomitant latex allergy. ISAC tests revealed in both cases sensitization to Bet v 1 homologues (PR-10 proteins) which are known to be responsible for numerous pollens-fruits reactions. Six patients had concomitant latex allergy including 2 positive for rHev b 6 in ISAC test and 5 positive in a least one determination in ImmunoCAP. One of latex positive patients had no concomitant allergies and responded in ISAC to rHev b 6, in ImmunoCAP – k82, Hev b 6.01, Hev b 6.02, Hev b 11. Five of latex responders had concomitant allergy to pollens with ($n = 2$) or without ($n = 3$) positive Bet v 1.

Clinical data and test results of patients with a history of food hypersensitivity are presented in detail in Table 4.

Discussion

Usefulness of the ISAC test has been demonstrated in several studies. Although varied in terms of inclusion criteria, application of additional tests and a panel of allergens analysed, they made it possible to understand mechanisms of allergic reactions in participants by indicating culprit determinants and, as a consequence, confirming cross-reactivity [13–16]. Scala *et al.* demonstrated relations between 75 components of ISAC in 23077 patients [17]. Ott *et al.* showed a high prevalence of sensitization to PR-10 proteins (allergens of birch, alder, apple, celery etc.) in patients with atopic dermatitis and allergic asthma [18, 19]. As far as latex allergy is con-

Table 3. Prevalence of sIgE against latex allergens in ImmunoCAP and ImmunoCAP ISAC tests in three study subgroups

	Allergen	Group A	Group B	Group C	
sIgE	Hev b 1	0 (0%)	1 (2.4%)	0 (0%)	
	Hev b 3	0 (0%)	1 (2.4%)	0 (0%)	
	Hev b 5	1 (2.6%)	1 (2.4%)	0 (0%)	
	Hev b 6.01	3 (7.7%)	1 (2.4%)	0 (0%)	
	Hev b 6.02	4 (10.3%)	1 (2.4%)	0 (0%)	
	Hev b 8	1 (2.6%)	4 (9.8%)	0 (0%)	
	Hev b 9	0 (0%)	1 (2.4%)	0 (0%)	
	Hev b 11	1 (2.6%)	1 (2.4%)	0 (0%)	
	ImmunoCAP ISAC	rHev b 1	0 (0%)	1 (2.4%)	0 (0%)
		rHev b 3	1 (2.6%)	0 (0%)	0 (0%)
rHev b 5		1 (2.6%)	0 (0%)	0 (0%)	
rHev b 6		4 (10.3%)	0 (0%)	0 (0%)	
rHev b 8		0 (0%)	1 (2.4%)	0 (0%)	

cerned, Raulf-Heimsoth *et al.* analyzed 19 patients with sIgE against chestnut and latex. rHev b 6.01 was found in 58%, rHev b 5 – 32%, rHev b 12 – 30.8%, rHev b 7.02 and 11 – 21%, rHev b 1 – 10.5% and rHev b 8 in 47% of subjects. A positive result for rHev b 8 (profilin) was interpreted as the cause of cross-reactivity [20].

During the recruitment into this study, the ISAC test's manufacturer changed the panel of allergens limiting latex allergens to Hev b 1, 3, 5, 6 and 8. The withdrawn allergens included Hev b 7 – patatin-like protein necessary to differentiate cross-reactions with potato, Hev b 11 – class I chitinase responsible for reactions with avocado, banana and chestnut, Hev b 9 (enolase) and Hev b 10 (superoxide dismutase Mn) – important in cross-reactions with fungi. Some of the significant food allergens, including banana, avocado, potato, tomato, were not included, either. Apart from Hev b 8, a family of profilins was represented only by pollens' allergens: Bet v 2, Mer a 1, Ole e 2, Phl p 12. No important food profilin was included e.g. Mal d 4, Api g 4 Acd d 9, Ara h 5. Another family important for cross-reactivity – lipid transfer proteins (LTP) – is represented by 4 allergens only – Art v 3, Cor a 8, Pru p 3, Par j 2. The only thaumatin-like protein is kiwi's Act d 2. In contrast, PR-10 proteins are richly represented by Bet v 1 homologues: Act d 8, Mal d 1, Ara h 8, Cor a 1.0101, Cor a 1.0401 etc. Although they do not cross-react with latex, they are useful for assessment of pollen-fruit reactions.

Lack of the aforementioned allergens is the major limitation of this study as it did not allow us to confirm all the possible cross-reactions. For the future studies in

Table 4. Results of skin prick tests (SPT), ImmunoCAP and ISAC tests in patients with a history of food allergy

No. of cases	History of allergy		SPT			ImmunoCAP					ISAC		
	Latex	Pollens	Latex	Food	Pollens	Latex k82	rHev b 6.01	rHev b 6.02	rHev b 8	rHev b 11	Food	rHev b 6	Bet v 1
Banana													
1	+	+	+	+	-	+	+	-	-	-	-	-	-
2	+	+	-	-	+	-	-	-	-	-	-	-	-
2	+	+	-	-	-	-	-	-	-	-	-	-	-
1	+	+	+	+	+	+	+	-	+	-	+	-	-
1	+	+	+	+	-	+	+	+	-	+	+	+	-
1	+	+	+	+	-	-	-	-	-	-	-	-	-
Kiwi fruit													
1	+	+	+	-	-	+	+	-	-	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	-	-	-
1	+	+	-	-	-	-	-	-	-	-	-	-	-
1	+	+	+	-	+	+	-	-	-	-	-	+	+
1	+	+	+	+	+	+	+	-	+	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	+	+	-	+	-	-	-	-	-	-	+	-	-
1	+	+	+	+	-	+	+	+	-	+	-	+	-
1	+	+	+	-	-	-	-	-	-	-	-	-	-
1	-	+	-	-	-	-	-	-	-	-	-	-	-
Avocado													
2	+	+	-	-	+	-	-	-	-	-	-	-	-
2	+	+	-	-	-	-	-	-	-	-	-	-	-
1	+	+	+	+	+	+	+	-	+	-	+	-	-
1	+	+	+	+	-	-	-	-	-	-	-	-	-
Potato													
1	+	+	+	-	+	+	-	-	-	-	-	+	+
1	+	+	+	+	+	+	+	-	+	-	+	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	+	+	+	+	-	+	+	+	-	+	+	+	-
1	-	+	-	-	-	-	-	-	-	-	-	-	-
Tomato													
1	+	+	+	+	-	+	+	-	-	-	-	-	-
2	-	+	-	-	+	-	-	-	-	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	+
1	-	+	-	+	+	-	-	-	-	-	-	-	-
Carrot													
1	+	+	+	-	+	-	-	-	-	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	-	-	-
Paprika													
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	+	-	+	-	-	-	-	-	-	-	-

Table 4. Cont.

No. of cases	History of allergy		SPT			ImmunoCAP					ISAC		
	Latex	Pollens	Latex	Food	Pollens	Latex k82	r Hev b 6.01	rHev b 6.02	rHev b 8	rHev b 11	Food	rHev b 6	Bet v 1
Celery													
1	-	+	-	+	+	-	-	-	-	-	+	-	-
1	+	+	+	-	+	+	+	-	+	-	-	-	-
2	+	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	+	+	-	-	-	-	-	-	-	-
1	-	+	-	+	+	-	-	-	-	-	-	-	+
1	+	+	+	+	-	+	+	+	-	+	-	+	-
1	-	+	-	+	+	+	-	-	-	-	+	-	-
Peanut													
1	-	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	-	-	+
Hazelnut													
1	-	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	-	-	+
1	+	+	+	+	+	+	-	-	-	-	+	+	+
1	+	+	+	-	+	+	+	-	+	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	+	+	-	-	-	-	-	+	-	+
1	-	+	-	-	+	-	-	-	-	-	+	-	+
1	+	+	+	+	+	-	-	-	-	-	-	-	-
1	+	+	+	+	-	+	+	+	-	+	-	+	-
1	-	+	-	+	+	+	-	-	-	-	+	-	-
1	+	-	-	-	-	-	-	-	-	-	-	-	-
1	+	+	+	+	+	-	-	-	-	-	+	-	+
1	-	+	+	+	+	+	-	-	-	-	+	-	-
1	-	+	-	-	-	-	-	-	-	-	-	-	-
Walnut													
1	-	+	-	-	+	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	-	-	+
1	+	+	+	-	+	+	-	-	-	-	-	+	+
1	+	+	+	-	+	+	+	-	+	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	-
2	+	+	+	-	+	-	-	-	-	-	-	-	+
1	+	+	+	-	+	-	-	-	-	-	-	-	-
1	+	+	+	+	-	+	+	+	-	+	-	+	-
1	-	+	-	+	+	+	-	-	-	-	+	-	-
1	+	-	-	-	-	-	-	-	-	-	-	-	-
1	-	+	+	+	+	+	-	-	-	-	+	-	-
1	-	+	-	-	-	-	-	-	-	-	-	-	-
Apple													
2	+	+	-	-	+	-	-	-	-	-	-	-	-
1	+	+	-	-	+	-	-	-	-	-	-	-	+
2	+	+	-	-	-	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	+	-	-
1	+	+	+	-	+	+	+	-	+	-	-	-	-
1	+	+	+	-	+	-	-	-	-	-	-	-	-
1	+	+	+	-	-	-	-	-	-	-	-	-	-
1	-	+	-	-	-	-	-	-	-	-	-	-	-
1	-	+	-	-	+	-	-	-	-	-	-	-	+

this area it would be useful to include LTPs: Hev b 12, Mus a 3, Api g 2, Act d 10, Ara h 9, Mal d 3, Lyc e 3, class I chitinases: Hev b 11, Pers a 1, Mus a 2 and thaumatin-like proteins: Mus a 4, Mal d 2, Pru p 2. Some of the missing allergens which could be useful for interpretation of cross-reactions may be determined separately with the use of ImmunoCAP. This is possible for Hev b 1, 3, 5, 6.01, 6.02, 8, 9, 11, Bet v 2, Phl p 12, Art v 3, Ara h 9 etc.

We included into this study 39 patients reporting immediate symptoms of latex allergy (group A), 41 allergic patients with no history of reaction to latex (group B) and 20 healthy controls (group C). Some participants (group A – 14, group B – 16) had also a history of food hypersensitivity which could result from cross-reactions between latex and fruit or pollens and fruit allergens. SPTs confirmed sensitization to latex in 16 and sIgE – in 12 patients only. The possible reasons for such overestimation were misinterpretation of symptoms by patients, reactions to other allergens or another mechanism of true latex allergy (i.e. T-cells mediated reactions). The low proportion of positive results was also found with food allergens. However, we have not performed double-blind placebo-controlled food challenges and based the diagnosis on SPT and sIgE that are not usually found in all cases of allergy to fruits [21].

sIgEs against latex allergens were found in symptomatic and asymptomatic patients with the following frequency: k82 – 18% and 12.2%, rHev b 5 – 2.6% and 2.4%; rHev b 6.01 – 7.7% and 2.4%; rHev b 6.02 – 10.3% and 2.4%; rHev b 11 – 2.6% and 2.4%, rHev b 8 – 2.6% and 9.8%, respectively. A higher prevalence of sIgE to profilin rHev b 8 in cases of clinically silent sensitization has been observed before [14, 16].

In group A, 4 patients were positive in the ISAC test for rHev b 6, one for rHev b 3 and 5, in the latter one – 1 patient was positive for rHev b 1 and 8. This is in contrast to the study of Ott *et al.* who found positive results for rHev b 6.02 in 69%, rHev b 5 – in 44%, rHev b 8 – 31%, rHev b 1 – 23% and rHev b 3 – in 2% of patients with latex allergy confirmed by SPT [16]. Similarly, Ebo *et al.* found a high prevalence of antibodies against rHev b 5 and/or 6.02 (75%) and relatively low against rHev b 1 and 3 (18%, 14% respectively) in the group of 22 patients with positive SPT and sIgE to latex [14]. We have not confirmed the fact of frequent co-existence of Hev b 11 and Hev b 6.02 either, what probably resulted from a low number of positive results.

Almost all the patients with latex allergy either had a history of food allergy or were asymptotically sensitized. Banana, avocado, potato and tomato were the most significant allergens. In some cases we managed to explain mechanisms of cross-reactivity. IgE against rHev b 11 was found in patients reacting to banana and avocado. IgE against rHev b 8 was revealed in cases of allergy to banana, kiwi fruit, avocado, potato and celery i.e. food containing homologous profilins [21, 22]. Profilin

Bet v 2 was positive in two patients, both with pollens allergy, with no history of latex or food allergy, but positive for rHev b 8 in ImmunoCAP.

Finally, the ISAC test made it possible to find alternative cross-reactions resulting in polyvalent allergy. In our study 9 cases of food allergy were associated with PR-10 proteins (Bet v 1 homologues).

Conclusions

ImmunoCAP ISAC test based on the CRD technique could be a valuable addition to the traditional allergological work-up, particularly in differentiating between latex-fruits and pollen-fruits cross-reactions. However, in cases of latex allergy, its advantages are significantly limited due to a small panel of available allergens.

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Conflict of interest

The authors declare no conflicts of interest.

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