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Determination of the Prevalence of Latex Sensitivity By in Vivo and in Vitro Methods Among Hospital Employees and Allergic Patients*

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Abstract: *Background:* Latex has been documented as causing immediate hypersensitivity reactions ranging from contact urticaria to severe anaphylaxis. The prevalence of latex allergy appears to be higher in certain risk groups due to increased exposure or to an increased intrinsic predilection for atopy.

The purpose of the present study was both to assess latex sensitivity in a large group of allergic patients and in hospital emyloyees and to evaluate the relationship between latex sensitivity and skin prick test (SPT) responses to fruits as well as inhalant allergens.

Methods: This study was designed prospectively in a randomized manner. SPTs were performed and specific IgE was assayed using ImmunoCAP System.

Results: Of the 102 allergic patients tested, 22 subjects (21.56%) and of the 205 hospital employees, 11 subjects (5.36%) werefound to have latex sensitivity with SPT and/or SpIgE. Three subjects (50%) in the latex +SPT hospital employees tested positive to aeroallergen(s) compared with 14 (14.89%) in the skin test negative group. In latex +SPT patients, all the subjects had positive tests to pollens and none showed any reaction to mite allergens and/or animal danders.

Conclusions: Considerable cross-reactivity between latex, aeroallergens and certain fruit allergens can be assumed as four subjects with latex sensitivity had positive SPT responses to banana, three to walnut, and two to kiwi extract, and most of them had positive tests mainly to grass mix extract.

Introduction

Immunoglobulin E (IgE) mediated hypersensitivity to natural rubber latex (NRL) has been recognized as an international medical problem due to the wide use of NRL products because of the universal precautions to prevent the spread of immunodeficiency virus. Probably, repeated exposure to latex together with genetic predisposition have led to latex sensitization (1-4). The immediate allergic reactions in latex hypersensitivity are caused by water-soluble latex antigens derived from the NRL of the rubber tree *Hevea brasiliensis*, as well as in manufactured products. It has been demonstrated that cornstarch powder, which is used as lubricant in latex gloves, can act as a carrier for latex antigens, inducing respiratory allergic reactions in sensitized patients (2, 5). Recently, cross-reactive allergenic proteins have been identified in banana, avocado, chestnut, kiwi (6-10).

If groups with high prevalence of latex allergy can be identified, cost effective latex avoidance measures can be taken to prevent severe allergic reactions (2, 11). Therefore, we have investigated latex sensitivity in allergic patients and in hospital employees. In this study, we also evaluated the relationship between latex and inhalant allergens as well as fruits.

Methods

Subjects; Group I consisted of 102 consecutively referred patients with a definite history of asthma and/or allergic rhinitis, urticaria, from adult allergy outpatient clinic. Group II comprised 205 hospital employees of whom 100 (Group IIa) were from surgical clinics (operating room, general surgery unit, gynecology and obstetrics, chest surgery, pediatric surgery, anesthesiology) of the University Hospital, Ankara, Turkey, with close contact with latex gloves, catheters, etc. and 102 (Group IIb) were recruited from medical clinics (pediatrics, psychiatry, respiratory medicine, physiotherapy and rehabilitation) with less exposure. Twentysix healthy controls without history of atopy and occupational-nonoccupational latex exprosure enrolled in

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Table 1. Occupational distribution of hospital employees

Occupation	Surgical Clinics	Medical Clinics	Total
Physicians	35	27	62
Nurses	30	40	70
Additional health care workers*	20	23	43
Laboratory technicians	9	3	12
Biologist	1	2	3
Housekeeping personnel	2	-2	
Clerical workers	3	2	5
Social workers	-	2	2
Psychologist	-	6	6
Total	100	105	205

*Additional health care workers AHW-A group of emplyoees who are doing housekeeping job, as well as transport and helping nurses.

Table 2. Demographic characteristics of study groups

	GROUP I (N=102)	GROUP IIa (N=100)	GROUP IIb (N=105)	CONTROLS (N=26)	*P* Value
Age (yr)§	32.60±10.95 (14-63)	31.20±8.66 (19-55)	33.22±8.78 (19-64)	27.42±2.92 (19-45)	>0.05
Sex (F/M)	54/48	39/61	74/31	11/15	
History of A,AR,E	102(100%)	41(41%)	30(28.57%)	-	<0.05*
Atopy#	102(100%)	18(18%)	13(12.38)	-	<0.05*
Dermatitis	-	36(36%)	8(7.6%)	2(7.7%)	<0.001**
Total IgE (kU/L)§	350.60±376.36 (18-2000)	98.34±105.76 (1-608)	158.23±309.56 (4-2000)	117.96±129.17 (1-582)	<0.01*
Phadiatop (+)	96(94.12%)	20(20%)	16(15.2%)	5(19.2%)	<0.01*
Years of hospital employment§		9.19±7.63 (0.4-32)	11.22±7.97 (6.7-38)		>0.05

§ Mean±SD

A-Asthma, AR-allergic rhinitis, E-Eczema

Atopy defines at least one positive SPT response to common aeroallergen extracts and a personal or family history of asthma, eczema or rhinitis.

* Statistically significant difference between Group I and other groups

** Statistically significant difference between Group IIa and Group IIb

this study. Subjects who fulfilled the criteria and consented to the study were interviewed to determine the status and years of employment, sex, frequency of using household latex gloves and the subject's clinical status. The study protocol was approved by the Ethics Committee of University of Ankara and written informed consent was obtained from all study participants.

Diagnostic tests;

SPTs; Skin tests were done by the prick through drop method on the volar surface of the forearm using a 25-gauge needle. Skin prick tests (SPTs) were performed with a group of 10 common aeroallergens (including mites, animal danders, pollens, mold mix) and with latex, banana, kiwi, walnut extracts (Stallergènes S.A.-Pasteur, France). No antihistamines were administered 6 wk prior to testing. Histamine hydrochoride 1mg/ml and phenolated glycerol-saline served as positive and negative controls. SPT responses were read at 15 minutes and considered positive when any reaction was greater than 50% of that induced by the histamine control.

In vitro tests; Serum samples collected from each subject for determination of total and specific IgE (SpIgE) were centrifuged, and stored at -20°C. SpIgE antibody was assayed by using the commercial ImmunoCAP System (Pharmacia, Uppsala, Sweden) only for the causal allergen that had been identified by SPT as well as for latex.

Statistics

Data analysis was performed using SPSS for Windows. Results are expressed as means±SD. Chi-

Table 3. Associated inhalant and fruit hypersensitivities in allergic patients (Group I) with a positive latex SPT response and/or latex specific IgE

			SPT response to								
						Common aeroallergens			fruit antigens		
Case	Age(yr) /Sex	Latex RAST* (kU/L)	Latex	Grass mix	Tree mix	Weed mix	*D.pt*	*D.far*	Banana	Kiwi	Walnut
1	56/M	11	+3	+4	-	+3	-	-	-	-	-
2	28/M	-	+3	+4	-	+4	-	-	+3	-	-
3	27/F	-	+3	+3	-	-	-	-	+3	-	+3
4	36/M	6.2	+3	+4	-	-	-	-	+3	-	-
5	32/F	-	+4	+4	+4	-	-	-	-	-	-
6	20/M	-	+4	+4	-	+4	-	-	-	+3	+4
7	32/F	-	+4	+4	-	-	-	-	+3	-	+3
8	50/M	-	+3	+4	+4	-	-	-	-	-	-
9	59/M	-	+3	+4	-	-	-	-	-	-	-
10	25/M	-	+3	+4	-	+3	-	-	-	-	-
11	37/F	1.2	-	-	-	-	+4	+4	-	-	-
12	33/M	8.8	-	-	+3	-	-	-	-	-	-
13	47/F	1.8	-	-	-	-	-	-	-	-	-
14	15/F	3.6	-	+4	-	+3	-	-	-	-	-
15	20/F	2.2	-	+4	-	+4	-	-	-	-	-
16	19/M	4.3	-	+4	-	+3	+4	-	-	-	-
17	17/M	15	-	+4	-	-	-	-	-	-	-
18	33/M	1.2	-	-	-	-	+4	-	-	-	-
19	16/M	4.4	-	+4	-	+4	-	-	-	-	-
20	34/M	4.2	-	+4	+4	-	-	-	-	-	-
21	15/F	4.1	-	+4	+4	+4	-	-	-	-	-
22	37/F	20	-	+4	+3	-	-	-	-	-	-

#A positive CAP System result is one greater than 0.35 kU/L

Square analysis was used to examine the association between skin test positivity to latex and the independent variables, and this was shown by kappa (κ). The differences between the means of two groups were analyzed by t-test and Mann-Whitney U test. Pearson analysis was used to calculate the correlations. Two-tailed *P* values was calculated with 95% confidence limits and a *P* value of <0.05 was regarded as significant.

Results

Occupational distribution of hospital personnel, the characteristics of the study groups and results are summarized in tables 1-4 and figure 1. None of the allergic subjects had any history of reactions to latex products, or more than one exposure to latex products in a medical or surgical setting. Similarly, in particular patients with +SPT responses to banana, walnut, kiwi, no histories of any adverse reactions to those foods thought to crossreact with latex were given. One patient claimed angiodemea after eating kiwi fruit, but found to have no latex sensitivity. All subjects with latex +SPT, all but three in +SpIgE patients were found to be sensitive to pollens (mainly to grass mix antigen $\kappa=0.139$) ($p>0.05$) as shown by SPTs.

Among Group IIa, eight latex sensitive subjects had no symptoms of latex allergy, but five claimed hand dermatitis (Table 4). Atopy was demonstrated in three of

Table 4. Associated inhalant and fruit hypersensitivities in allergic patients (Group I) with a positive latex SPT response and/or latex specific IgE

						SPT response to						
						Common aeroallergens				fruit antigens		
Case	Age(yr) /Sex	Occupation (Clinic)	Dermatitis	Latex CAP# (kU/L)	Latex	Grass mix	Tree mix	Weed mix	*D.pt*	Banana	Kiwi	Walnut
1	21/F	Nurse (OR)	+	3.5	+4	-	-	-	-	-	-	-
2	26/F	Nurse (OR)	+	3.1	+4	-	-	-	-	-	-	-
3	31/F	Nurse (OR)	+	-	+4	-	-	-	+4	-	+4	-
4	28/M	Physician (CS)	+	-	+4	-	-	-	-	-	-	-
5	28/M	Physician (A)	-	-	+4	+4	-	+3	-	-	-	-
6	24/F	Nurse (OR)	+	-	+4	+4	+3	-	-	-	-	-
7	24/F	Nurse (OR)	1.3	-	-	-	-	-	-	-	-	-
8	29/F	Physician (A)	-	10	-	-	-	-	-	-	-	-
9	38/F	AHW* (Ped)	-	5.6	-	-	-	-	-	-	-	-
10	33/F	Psychologist (P)	-	2	-	-	-	-	-	-	-	-
11	47/M	AHW* (RM)	+	3.1	-	-	-	-	-	-	-	-

#A positive CAP System result is one greater than 0.35 kU/L

*AHW-Additional health care workers-A group of employees who are doing house keeping job, as well as transport and helping nurses.

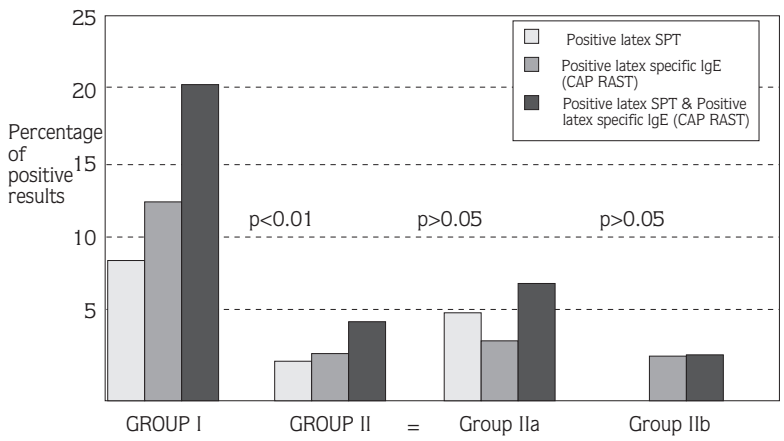

Figure 1. Results of latex sensitivity in atopic patients and hospital employees

*Group II=Group IIa + Group IIb

six subjects (50%) with +SPT to latex, as compared with 14 of 94 subjects (14.89%) with -SPT ($p<0.05$), the prevalence of latex sensitivity among atopic hospital employees being 16.66%. Although no +SPT reactivity was found in Group IIb, three had+SpIgE to latex. None in control group showed either positive SPT response to

latex or SpIgE measurement. In our series the overall correlation between the two diagnostic methods used for the evaluation of latex allergy was κ=0.167. Overall 22 (21.56%) of 102 allergic patients and 11 (5.36%) of 205 hospital personnel were latex sensitive, being significantly high in atopics ($p<0.05$). Latex sensitiviy in Group I was significantly different from others (except Group IIa) as shown with both latex +SPT and +SpIgE ($p<0.01$) (Figure 1). Although the prevalence of latex sensitivity is higher in Group IIa, the difference between IIa and IIb was not statistically significant ($p>0.05$).

When "Latex positive" and "Latex negative" groups, based on SPT s and/or SpIgE results were compared, the variables with no statistical significance ($p>0.05$) included age, duration of allergic symptoms (for patients), year of hospital experience (for employees), and serum total IgE levels. No relationship was observed between latex +SPT and eczema on hands, frequency or work related with glove-wearing. However, the percentage of skin reactions to latex was five times higher in hospital employees with atopy (8.82%) than in hospital employees without atopy (1.75%). There was no significant difference between the study groups in the status of employment. However, the higher prevalence of latex sensitivity was in operating room nurses both with SPT and SpIgE assays 13.3% and 10% respectively).

Discussion

In the last decade, there have been many reports of latex IgE-mediated reactions reflecting a dramatic increase in incidence, related to changes both in usage and manufacturing methods (1-3, 12, 13). Our results show that a significant proportion of patients in hospital based allergy practice has positive SPT responses to latex, although they were not referred because of symptoms attributed to latex. In Group I allergic patients, 21.56% had latex sensitivity either with +SPT and/or CAP RAST. When the studies about latex sensitivity in allergic patients are surveyed, the results of the diagnostic methods, SPTs or SpIgE, range between 4.2%-12% (14-16). Summing of the two methods besides careful selection of Group I may explain the higher prevalence rates of latex sensitivity in our study.

Latex sensitivity was significantly higher among atopic patients with symptomatic allergy, compared with hospital personnel, and a comparable difference was also observed between these groups and healthy control subjects. In this study, the prevalence of latex +SPT in hospital employees (2.92%) is lower compared with the previous report (17-21). One of the major differences is that our group consisted of all kinds of hospital personnel with different employment equally, since the frequency of glove wearing varies. Alternatively, in other studies performed by different investigators, more symptomatic emplyoees may have been participated, by contrast in our study, we tried to avoid this voluntary participation by inviting all employees. Another possible explanation for the difference in response rates between ours and literature may reflect various allergen content in the latex extract used, since allergenicity varies from one product to another (18, 22).

Host and environmental factors, including atopy and high levels of exposure both occupational and nonoccupational, can predispose to immunologic sensitization to latex. Logistic regression analysis indicated that atopy was the principal determinant for the development of latex sensitivity even without known exposure (1, 4, 13). The higher prevalence of latex allergy found among operating room nurses, especially atopics supports this. Furthermore, 50% of latex +SPT employees were positive to at least one common inhalant allergen supporting a diagnosis of atopy. In this survey, none of the latex positive individuals reported any symptoms related to latex. Also, the lack of correlation between itching of the hands during glove wearing and latex sensitivity may be linked to the fact that the degree of sensitization is low. Patient surveys and chart reviews were not able to identify recurrent latex exposure in our group of patients.

The most striking finding in this study was that most of the latex +SPT cases had positive tests mainly to grass mix pollen extract. This data suggests that either latex exposure is more common than expected, or that the antigens found in NRL may be immunologically cross-reactive with other antigens; fruits like banana, avocado, kiwi and/or pollens like ragweed and blue grass (7, 9, 10, 20, 24). This was confirmed in our study, in a range of 10%-40%, changing with the fruits used. At present it seems reasonable that patients known to be allergic to any of these fruits should be advised about the potential risks for developing allergic reactions with NRL products. Our finding that 50% of the latex +SPT group tested positive to one or more aeroallergens compared with 14.89% in -SPT group, also raises the suggestion of utilizing aeroallergen skin tests - thinking of atopy as a high risk factor and probable crossreactive determinants between pollens and latex- in screening healthcare workers prior to any elective surgical or medical procedure. Whatever the result of the aeroallergen test and history, in vivo or in vitro determination of latex sensitivity is needed to detect the possibility of IgE-

mediated latex allergy (25). In our experience, latex SPT with standardized extract is safe, cheap and easy to perform. In vitro tests offer greater safety but they are less sensitive (2, 21). It is noteworthy that the proportion of positive RAST in individuals with +SPT are 1/5 and 1/3 in Group I and Group II, respectively, with the use of the CAP system, which is known to be more sensitive than the conventional RAST, as reported in other series (24-26).

Although the predictive value of a +SPT to latex is not known, sensitivity to latex is common enough to warrant systematic preoperative screening in healthcare workers. However the diagnosis of clinically relevant allergy depends, in the first instance, on a correlation between the clinical history and the results of skin tests. Thus, when a patient whose history is not definitive for latex allergy has +SPT response -crossreactive allergens may account for positive tests- determining cutoff values for SPTs, for in vitro tests, and for both must have been used, as recently suggested for common aeroallergens (27).

As reported previously, latex sensitization is thought to be morecommon than suspected before. And the only present treatment in symptomatic latex +SPT allergic patients is avoidance (2, 28). Occupational allergic diseases caused by latex may lead to permanent disability, even after removal from exposure. The development of a comprehensive approach to safeguarding patients and healthcare workers should be wieved as an urgent priority. Moreover, the costs of initiating these proposals would appear to be small in comparison to the savings expected from reducing the administrative, medical, disability, and liability costs of latex allergy (11).

In conclusion, in vivo tests may detect latex sensitization in atopic patients with no history of recurrent latex exposure and in hospital employees with a well defined history of recurrent latex exposure or adverse reactions to latex. When skin testing is unavailable, and in the presence of negative in vitro latex tests, precautionary latex avoidance measures should be undertaken empirically. More studies are also warranted to identify subjects who are at risk for developing latex allergy.

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