

Profile of Latex Sensitization and Allergies in Children and Adolescents With Myelomeningocele in São Paulo, Brazil

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■ Abstract

Background: Latex allergy is an important cause of occupational allergy. In many countries the prevalence of latex allergy is still high and the profile of latex sensitization is unknown.

Objectives: To evaluate the frequency of sensitization and allergy to latex in children and adolescents with myelomeningocele and to identify associated risk factors.

Methods: The study included 55 children and adolescents with myelomeningocele followed at a specialized center. In addition to a standard questionnaire and skin prick tests (SPTs) to aeroallergens and total latex, the patients underwent determination of total and specific serum IgE to latex and recombinant allergens.

Results: We observed a prevalence of 25% for latex sensitization and of 20% for latex allergy. Twenty-four patients (43.6%) were atopic and the average age for the first reaction to latex was 44.5 months. Cutaneous reactions were the most frequently reported reactions (72.7%). Specific immunoglobulin (Ig) E to rHev b 1, rHev b 3, rHev b 5, rHev b 6.1, and rHev b 6.2 was detected in over 50% of patients allergic to latex. Multivariate analysis showed current asthma, atopy, and having undergone 4 or more operations to be risk factors for latex sensitization.

Conclusions: Our study documented a high prevalence of sensitization and allergy to latex in patients with myelomeningocele. Specific IgE to rHev b 1, rHev b 3, rHev b 5, rHev b 6.1, and rHev b 6.2 was detected in over 50% of children and adolescents with myelomeningocele who are allergic to latex. A history of current asthma, atopy, and having undergone 4 or more operations were independent risk factors for latex allergy.

Key words: Allergy. Latex. Myelomeningocele. Recombinant allergens. Brazil.

■ Resumen

Introducción: La alergia al látex constituye una causa importante de alergia ocupacional. En muchos países la prevalencia de alergia al látex es elevada y su perfil de sensibilización desconocido.

Objetivos: El objetivo de este estudio fue evaluar la frecuencia de sensibilización y de alergia al látex en niños y adolescentes con mielomeningocele e identificar los factores de riesgo asociados.

Métodos: Este estudio evaluó 55 niños y adolescentes afectados de mielomeningocele y monitorizados en un centro especializado. Se realizó un estudio de test cutáneos (prick) frente a aeroalérgenos y látex total. Así como un cuestionario y la determinación de IgE total y específica frente a látex y sus alérgenos recombinantes.

Resultados: En los resultados encontramos un 25% de sensibilización y un 20% de alergia al látex. Un 43.6% de los pacientes eran atópicos y la edad media de comienzo de la sintomatología fue de 44.5 meses, siendo las reacciones cutáneas las más frecuentes (72.7%). La IgE específica frente a r Hev b 1, 3, 5, 6.1 y 6.2 se detectó en más del 50% de los pacientes alérgicos al látex. El análisis multivariante mostró como significativas las siguientes variables: asma, atopia, y número de cirugías a las que había sido sometido el paciente.

Conclusiones: Como conclusión este estudio documenta una elevada prevalencia de sensibilización y alergia al látex en pacientes con mielomeningocele. La IgE específica frente a r Hev b 1, 3, 5, 6.1 y 6.2 se detecta en más del 50% de los alérgicos al látex en esta serie. Entre los factores independientes de riesgo para sufrir alergia a látex se encuentran el asma, la atopia y el haber estado sometido a más de cuatro cirugías.

Palabras clave: Alergia. Látex. Mielomeningocele. Alérgenos recombinantes. Brasil.

Introduction

Latex allergy is an important cause of occupational allergy and is responsible for numerous allergic reactions in sensitized individuals [1]. It manifests as a type 1 hypersensitivity reaction, mediated by immunoglobulin (Ig) E antibodies, with urticaria, angioedema, rhinitis, conjunctivitis, asthma, eosinophilic meningitis, and anaphylaxis [1,2]. Severe systemic reactions usually occur after mucosal exposure to products containing latex or during surgical procedures, but they may also occur in several circumstances in daily life [3]. Fourteen latex allergens have been characterized and denominated Hev b 1 to 14 [4].

In some countries the prevalence of latex allergy in individuals with usual risks (health care workers and patients with spina bifida) has been decreasing due to increased control of exposure to latex [5-7]. However, new risk groups have been identified, such as gardeners, cooks, beauticians, and civil construction workers, all of whom use latex gloves frequently [8,9]. The prevalence of latex allergy in children with myelomeningocele, who, from an early age are frequently manipulated during surgery, ranges from 1% to 72% [10,11]; these children are generally sensitized to allergens Hev b 1, Hev b 3, and Hev b 7 [12-14].

Few studies have analyzed latex sensitization and allergy in Brazil and those that have focused mainly on health professionals [15,16]. Just 1 study has evaluated patients with myelomeningocele but it did not evaluate sensitization to latex allergens [17].

The objectives of this study were to assess the prevalence of latex sensitization and allergy in patients with myelomeningocele from a specialized center and to identify associated risk factors.

Methods

Patients

Fifty-five children and adolescents with myelomeningocele treated in the department of neurosurgery of the Federal University of São Paulo in Brazil from October 2007 to October 2008 were analyzed. They were aged between 9 months and 14 years (mean, 7.3 years), 56.4% were female, and they had all undergone surgical repair of myelomeningocele with or without ventriculoperitoneal shunting (VPS). They were followed for at least 6 months in all cases.

The patients' parents or guardians were asked if their children had allergic diseases or symptoms, prior personal or family conditions related to corrective surgery of the myelomeningocele, or a current history of reaction to latex. Data regarding previous surgical procedures were obtained from medical records. The patients then underwent skin prick testing (SPT) and blood samples were obtained for determination of specific IgE to latex and recombinant latex allergens.

The study was approved by the ethics committee at our hospital. All the patients and their parents or guardians were informed of the nature of the study and signed an informed

consent form. Exclusion criteria for the study were continuous use of antihistamines or oral corticosteroids.

Characterization of Associated Allergic Disease

The International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire was used to characterize allergic disease. Current asthmatics were identified as those who responded affirmatively to the question "have you had wheezing in the past 12 months?" and severe asthmatics as those who responded affirmatively to the above question and at least 2 of the following questions: "have you had 4 or more attacks of wheezing in the past 12 months?", "has your sleep been disturbed by wheezing at least one night a week in the past 12 months?", "has wheezing ever been severe enough to limit your speech to only one or two words between breaths in the past 12 months?", and "has your chest sounded wheezy during or after exercise in the past 12 months" [18].

Patients were diagnosed with current rhinitis and current rhinoconjunctivitis when they answered "yes" to the questions "have you ever had a problem with sneezing or a runny or blocked nose when you did not have a cold or the flu in the past 12 months" and "have you had a problem with sneezing or a runny or blocked nose accompanied by itchy-watery eyes when you did not have a cold or the flu in the past 12 months". Severe rhinoconjunctivitis was characterized by impairment of daily activities due to nose problems among those with current rhinoconjunctivitis [18].

Patients who answered "yes" to the question "Have you ever had an itchy rash which was coming and going for at least six months?" were diagnosed with eczema. Those who additionally answered "yes" to the question "Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?" (combined criterion for eczema) and "have you been kept awake at night by this itchy rash" were identified as having severe eczema [18].

Urticaria was diagnosed in patients who reported having had a rash or all-over body itching that moved around and was transient; angioedema, in turn, was diagnosed in those who reported having had swelling in the region of the eyes, mouth, hands, or genitals [19].

Patients with a history of clinical features suggesting an IgE-mediated reaction after contact with latex (rubber products such as bladder catheters, gloves, catheters, drains, masks, and anesthesia) were considered to have a positive history of latex allergy.

Identification of Allergic Etiology: IgE-Specific Research

In vivo tests. Patients underwent SPT with the following allergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, *Blattella germanica*, *Periplaneta americana*, dog and cat dander, mixed grasses, mixed fungi, and total latex (Laboratório IPI-ASAC). Histamine solution (10 mg/mL) and saline were used as a positive and negative control, respectively. The SPT was considered positive if the patient developed a wheal with a mean diameter of at least 3 mm.

In vitro tests. Serum concentrations of total IgE and specific IgE to latex and to individual recombinant latex allergens (rHev b 1, rHev b 3, rHev b 5, rHev b 6.01, rHev b 6.02, rHev b 8, rHev b 9, and rHev b 11) were determined by enzyme immunoassay (UniCAP). Values were expressed in kU/L and evaluated according to the reference ranges recommended by the manufacturer. Specific IgE values equal to or greater than 0.7 kU/L (Class 2) were considered positive. We used a cutoff of 0.70 kU/L rather than 0.35 kU/L in an effort to increase the specificity of the test.

Patients were considered to be sensitized when they had specific serum IgE or a positive SPT to latex without clinical manifestations, allergic when they developed clinical manifestations following contact with latex, and atopic when they had a positive SPT to other allergens.

Statistical Analysis

The study groups were divided into sensitized and allergic (S+A) individuals and nonsensitized (NS) individuals. Depending on the nature of the variables, parametric or nonparametric tests were used, and 5% was set as the criterion for rejecting the null hypothesis. Variables observed to be significant in the univariate analysis were analyzed by multivariate logistic regression analysis (SPSS version 17.0).

Results

Twenty-five patients (45%) were either sensitized (n=14, 25%) or allergic (n=11, 20%) to latex (S+A group). Table 1 shows the clinical characteristics of the patients according to the group they belonged to. The following variables were all significantly more frequent in the S+A group than in the NS group: a history of 4 or more operations, use of VPS, diagnosis of angioedema and current rhinitis, atopy, and total IgE of over 200 kU/L. Patients in the S+A group had also undergone a significantly higher number of operations.

Of the 11 patients allergic to latex, 6 (54.5%) had cutaneous symptoms only (eg, urticaria or angioedema); 3 (27.3%) had respiratory symptoms only (eg, wheezing or rhinoconjunctivitis); and 2 (18.2%) had both cutaneous

and respiratory symptoms. The mean age of the patients when they experienced their first reaction to latex was 44.5 months (range, 2-80 months); only 1 patient (9.1%) had had a reaction before 12 months of age. Two patients (18.2%) had had a reaction in the past 12 months and 2 had been hospitalized due to a severe reaction.

Table 2 shows the distribution of latex and allergen-specific IgE results by group. We observed a larger number of positive latex allergens in allergic patients than in sensitized patients.

The concordance between positive SPT results and specific IgE to latex and recombinant latex allergens is shown in Table 3.

Nineteen S+A patients (76%) had a positive SPT and

Table 1. Descriptive and Comparative Analysis of Myelomeningocele Patients With and Without Latex Sensitization or Allergy^a

	Latex Sensitization and Allergy		P Value
	Yes (n=25)	No. (n=30)	
Average age, y	8.0	6.7	.202 ^b
Male	11 (44.0)	13 (43.3)	1.000 ^c
Personal history of atopy	16 (64.0) ^d	8 (26.7)	.007 ^c
Current asthma	11 (44.0)	6 (20.0)	.080 ^c
Severe asthma	1 (4.0)	2 (6.7)	1.000 ^c
Current rhinitis	19 (76.0) ^d	14 (46.7)	.032 ^c
Current rhinoconjunctivitis	14 (56.0)	8 (26.7)	.052 ^c
Severe rhinoconjunctivitis	1 (4.0)	1 (3.3)	1.000 ^c
Current eczema	2 (8.0)	3 (10.0)	1.000 ^c
Eczema (combined criterion)	1 (4.0)	3 (10.0)	.617 ^c
Severe eczema	1 (4.0)	2 (6.7)	1.000 ^c
Urticaria	6 (24.0)	4 (13.3)	.484 ^c
Angioedema	8 (32.0) ^d	2 (6.7)	.032 ^c
Average operations, No.	6.2 ^d	3.0	<.001 ^b
≥4 operations	16 (64.0) [*]	10 (33.3)	.032 ^c
Average age at time of first operation, d	4.4	9.1	.994 ^b
Use of catheter	19 (76.0)	18 (60)	.257 ^c
Average duration of catheter usage, d	222.9	344.7	.398 ^b
Presence of VPS	21 (84.0) ^d	17 (56.7)	.041 ^c
Family history of atopy	14 (56.0)	18 (60.0)	.790 ^c
Total IgE >200 kU/L	16 (64.0) ^d	9 (30.0)	.016 ^c
Allergens identified via SPT			
<i>Dermatophagoides pteronyssinus</i>	12 (48.0)	7 (23.3)	
<i>Dermatophagoides farinae</i>	9 (36.0)	6 (20.0)	
<i>Blomia tropicalis</i>	11 (44.0)	5 (16.7)	
<i>Blattella germanica</i>	1 (4.0)	0	
<i>Periplaneta americana</i>	1 (4.0)	0	
Dog dander	0	0	
Cat dander	4 (16)	0	
Mold mix	2 (8.0)	1 (3.3)	
Grass mix	2 (8.0)	0	

Abbreviations: IgE, immunoglobulin E; SPT, skin prick test; VPS, ventriculoperitoneal shunt.

^aData are shown as number (%) of patients unless otherwise specified.

^bCalculated using Mann-Whitney U test.

^cCalculated using Fisher exact test.

^dSignificant values.

Table 2. Frequency of Positive Skin Prick Tests to Latex and Specific Immunoglobulin (Ig) E (\geq class 2) to Latex and Recombinant Allergens in Latex-Allergic and Latex-Sensitized Patients^a

	Allergic (n=11)	Sensitized (n=14)	Sensitized and Allergic (n=25)
Positive SPT	11 (100)	8 (57.1)	19 (76.0)
Specific IgE \geq 0.70 kU/L			
Latex	11 (100.0)	8 (57.1)	19 (76.0)
rHev b 1	10 (90.9)	6 (42.9)	16 (64.0)
rHev b 3	6 (54.5)	5 (35.7)	11 (44.0)
rHev b 5	7 (63.6)	3 (21.4)	10 (40.0)
rHev b 6.01	8 (72.7)	4 (28.6)	12 (48.0)
rHev b 6.02	8 (72.7)	6 (42.9)	14 (56.0)
rHev b 8	1 (9.1)	1 (7.1)	2 (8.0)
rHev b 9	3 (27.3)	5 (35.7)	8 (32.0)
rHev b 11	3 (27.3)	7 (50.0)	10 (40.0)

Abbreviation: rHev b: recombinant *Hevea brasiliensis*.

^aData are shown as number (%) of patients.

Table 3. Kappa Concordance Coefficient Between Positive Skin Prick Tests (SPT) to Latex, Specific Immunoglobulin (Ig) to Latex, and Recombinant Allergens in Patients Sensitized and Allergic to Latex

	SPT Total Latex	IgE Total Latex	IgE rHev b1	IgE rHev b3	IgE rHev b5	IgE rHev b6.01	IgE rHev b6.02	IgE rHev b8	IgE rHev b9	IgE rHev b11
SPT total latex		1	0.72	0.64	0.64	0.68	0.49	0.18	0.24	0.23
IgE total latex	1		0.72	0.64	0.64	0.68	0.49	0.18	0.24	0.23

Table 4. Comparative Analysis of Patients According to the Presence or Absence of a History of Clinical Reaction To Latex^a

	History of Clinical Reaction to Latex		P Value
	Positive (n=14)	Negative (n=41)	
Average age, mo	100	84	.258 ^b
Male	5 (35.7)	19 (46.3)	.547 ^c
Personal history of atopy	10 (71.4) ^d	15 (36.6)	.032 ^c
Current asthma	8 (57.1) ^d	9 (22.0)	.021 ^c
Severe asthma	2 (14.3)	1 (2.4)	.156 ^c
Current rhinitis	10 (71.4)	23 (56.1)	.361 ^c
Current rhinoconjunctivitis	9 (64.3)	13 (31.7)	.056 ^c
Severe rhinoconjunctivitis	2 (14.3)	0	.061 ^c
Current eczema	4 (28.6) ^d	1 (2.4)	.012 ^c
Eczema (combined criterion)	3 (21.4) ^d	1 (2.4)	.047 ^c
Severe eczema	3 (21.4) ^d	0	.014 ^c
Urticaria	4 (28.6)	6 (14.6)	.255 ^c
Angioedema	6 (42.9) ^d	4 (9.8)	.012
Average operations, No.	6.4 ^d	3.8	.031 ^b
\geq 4 operations	9 (64.3)	17 (41.5)	.215

Table 4. Continued

	History of Clinical Reaction to Latex		P Value
	Positive (n=14)	Negative (n=41)	
Age at time of first operation, d	2.7	8.9	.692 ^b
Use of catheters	8 (57.1)	29 (70.7)	.510 ^c
Average duration of catheter usage, d	45	372.7	.283 ^b
Use of VPS	11 (78.6)	27 (65.9)	.510 ^c
Family history of atopy	9 (64.3)	23 (56.1)	.756 ^c
Mean total and specific Serum IgE			
Latex	28.4 ^d	3.4	<.001 ^c
rHev b 1	11.7 ^d	0.8	.001 ^c
rHev b 3	5.8	2.8	.149 ^c
rHev b 5	21.2 ^d	0.3	.025 ^c
rHev b 6.01	3.8 ^d	0.4	.016 ^c
rHev b 6.02	2.7 ^d	0.6	.036 ^c
rHev b 8	0.1	0.1	.775 ^c
rHev b 9	0.2	0.1	.515 ^c
rHev b 11	0.5	0.3	.699 ^c
Total IgE	1008.0 ^d	375.7	.042 ^c

^aData are shown as number (%) of patients unless otherwise specified.

^bCalculated using Mann-Whitney U test.

^cCalculated using Fisher exact test.

^dSignificant values.

specific IgE to latex, and 25 (100%) had positive specific IgE to at least 1 of the recombinant allergens studied. Specific IgE to rHev b 1 was detected in 16 patients (64%) and to rHev b 6.02 in 14 patients (56%) (Table 2).

Of the 14 patients with a history of reaction to latex, 3 were included in the NS group. On comparing patients according to whether or not they had a history of reaction to latex, statistically significant differences were observed for atopy, current asthma, current eczema, eczema (combined criterion), severe eczema, average number of operations undergone, total serum IgE levels, and specific IgE to latex, rHev b 1, rHev b 5, rHev b 6.01, and rHev b 6.02 (Table 4).

On analyzing patients according to the average number of operations undergone, we found that in the S+A group the mean values of total and specific IgE to latex and its allergens were higher in those who had undergone 4 or more operations, with statistically significant differences found for rHev b 5 and rHev b 6.01 (Table 5).

A diagnosis of current asthma, atopy, and having undergone 4 or more operations were all identified as independent risk factors for latex allergy (Table 6).

Table 5. Average Values of Total and Specific Immunoglobulin (Ig) E to Latex and Recombinant Allergens (average kU/L) According to the Number of Operations in Patients Sensitized and Allergic to Latex

Specific IgE	No. of Operations		P Value ^a
	<4	≥4	
Latex	5.3	31.9	.054
rHev b 1	4.0	10.0	.444
rHev b 3	1.5	11.7	.156
rHev b 5	0.2	24 ^b	.044
rHev b 6.01	0.6	4.2 ^b	.022
rHev b 6.02	0.9	3.5	.133
rHev b 8	0	0.1	.625
rHev b 9	0.2	0.3	.550
rHev b 11	0.4	0.8	.477
Total IgE	444.1	1203.8	.336

Abbreviation: rHev b, recombinant *Hevea brasiliensis*.

^aCalculated using the Mann-Whitney U test.

^bSignificant values.

Table 6. Factors Associated With the Diagnosis of Latex Allergy Identified by Logistic Regression

	Odds Ratio	95% CI	P Value
Current asthma	5.9	1.4-24.5	.014
Atopy	2.4	1.9-14.1	.005
≥4 operations	1.4	1.1-1.7	.003

Discussion

Patients with myelomeningocele have several known risk factors for latex sensitization. They undergo multiple operations early in life involving the manipulation of the peritoneum, mucous membranes, and meninges, and are often subject to exposure to latex-containing products, such as probes, catheters, and gloves. There is also evidence that myelomeningocele itself might be a risk factor for latex sensitization [20].

The frequency of sensitization (25%) and allergy (20%) to latex observed in the present study is similar to figures reported by other authors [11]. Also consistent with previous reports, we observed no differences in prevalence between males and females [3].

The main symptoms reported by patients with latex allergy were skin reactions (72.7%), coinciding with other reports [21]. Two patients (18.2%) had a severe reaction requiring hospitalization. None of these events occurred during surgery, even though latex allergy has been identified as the second leading cause of intraoperative anaphylaxis, after muscle relaxant drugs [22].

There are few reports on the mean age of onset of symptoms of latex allergy but the figures available range from 5 [23] to 12.5 years [24]. In our study it was 3.7 years. It has been suggested that sensitization to latex increases with age due to increasing exposure to latex during additional operations [3,24].

In our study the following factors were all significantly more frequent in patients sensitized to latex: having undergone 4 or more operations, use of VPS, a history of atopy, and a total IgE level of above 200 kU/L. Number of operations, especially in the first year of life, seems to be the most important risk factor for sensitization and is directly related to higher levels of specific IgE to latex [24-27]. Although VPS devices do not contain latex, they have been identified as a risk factor for latex sensitization, possibly due to the number of operations needed to correct the functioning of these devices [28].

Like other investigators, we found that a personal history of atopy (asthma, rhinoconjunctivitis, and rhinitis), but not a family one was a risk factor for latex sensitization [29].

None of the patients in our series, even those with a history of hospitalization due to severe reactions to latex, developed a reaction during SPT. However, it is recommended that SPT in such cases should be performed in a hospital, especially in patients with a history of severe reactions [30,31].

All patients diagnosed as sensitized to latex had a positive SPT and positive specific IgE to latex. This total concordance between the tests increases the possibility of using either of them to detect the presence of specific IgE to latex.

In the S+A group the frequency of positive results obtained by SPT and total IgE and latex allergens was higher, especially for SPT, total IgE, latex and its allergens rHev b 1, rHev b 3, rHev b 5, rHev b 6.01, and rHev b 6.02 (Table 2). In addition, SPT and measurement of specific IgE to latex and some of its allergens (rHev b 1, rHev b 3, rHev b 5, rHev b 6.01, and rHev b 6.02) showed good agreement (Table 3). These data show good concordance between these tests and suggest that either can be used for the diagnosis of sensitization to latex allergens.

Health care workers are generally sensitized to Hev b 2, Hev b 5, Hev b 6.2, and Hev b 13, while patients with spina bifida tend to be sensitized to Hev b 1, Hev b 3, and Hev b 7 [16,17]. In the S+A group we found rHev b 1 and rHev b 6.2 to be involved in the sensitization of over 50% of patients (the criterion used to define the major allergen), and rHev b 3, rHev b 5, rHev b 6.01, and rHev b 11 to be involved in at least 40% of cases.

As expected, the vast majority (90.9%) of patients with myelomeningocele and latex allergy had positive specific IgE to rHev b 1 [45]. The higher frequency of specific IgE to rHev b 6.01, rHev b 6.02, and rHev b 5 than to rHev b 3 in our study was a surprise, since the opposite has been reported [12,33].

Patients who had undergone 4 or more surgical procedures had higher mean total IgE and specific IgE to latex and its allergens (mainly rHev b 5 and rHev b 6.01). Although several studies have related an increased number of operations to higher levels of total and specific IgE to latex, there has been no mention of a relationship with specific allergens [3,24,28]. Might it be that rHev b 5, and rHev b 6.01 are the first allergens to appear in latex-allergic patients who undergo multiple surgical procedures? Or might the difference we detected be due to our small sample size and therefore lack of clinical significance?

Multivariate analysis showed that a diagnosis of current asthma, atopy, and a history of having undergone 4 or more operations were all significant risk factors for latex allergy in myelomeningocele patients, coinciding with reports in the literature [1,10,20,34,35].

Conclusions

We have documented a high prevalence of sensitization (25%) and allergy (20%) to latex in children and adolescents with myelomeningocele. SPT and specific serum IgE to latex performed similarly in the identification of sensitization to latex. The most common recombinant allergens identified were rHev b 1, rHev b 3, rHev b 5, rHev b 6.01, and rHev b 6.02. A history of 4 or more surgical procedures and a personal history of current asthma, rhinitis, or rhinoconjunctivitis were found to be independent risk factors for latex sensitization. Control of environmental factors (exposure to latex) is still the main recommendation in myelomeningocele patients who are allergic to latex.

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