

Prevalence of latex sensitization and allergy in Portuguese children

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The prevalence of latex allergy has been increasing not only in risk groups but also in the general population, where it is accepted to average 1%. In children, latex sensitization prevalence studies are scarce and involve different population sampling and allergy testing methods, which makes it difficult to compare across studies. Nevertheless, existing studies point towards a low prevalence of latex allergy in children, which still needs to be confirmed in the Portuguese population. Aiming at studying the prevalence of latex sensitization and allergy in a sample of Portuguese children, we studied 182 children from two different hospital outpatient clinics. A standardized questionnaire focusing on atopic background, previous history and allergic signs or symptoms on exposure to latex or fruits was given to all children and parents. Skin prick testing was performed with a battery of common aeroallergens as well as latex. Serum total IgE, Phadiatop, F × 5E and latex-specific IgE were determined in all children. Specific IgE to latex-crossreacting fruits was determined in latex-sensitized children. Based upon the questionnaire, the prevalence of latex allergy would be 0.5%. The prevalence of latex sensitization would be 3.8%, when based solely upon skin prick testing, and 12.1% (≥ 0.35 IU/ml) or 6.6% (≥ 0.70 IU/ml) when based singly upon determination of latex-specific IgE. When positive results for either test were considered, the prevalence of latex sensitization was 14.3%. All latex-sensitized children were atopic. Sensitivity to latex-crossreacting foodstuffs was demonstrated in 61.5% of latex-sensitized children (16/26). This study shows that the prevalence of latex allergy and sensitization in Portuguese atopic and non-atopic children, as analysed using various diagnostic methods, is similar to that observed in other countries. In addition, the assessment of latex allergy and sensitization should always include skin prick testing and determination of serum IgE.

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Latex allergy was virtually unknown until 1980s, and is currently regarded as a serious health problem in view of its social and labour repercussions. Its prevalence has been increasing in particular groups. In the general population the prevalence is accepted to average about 1% (1).

A carefully taken clinical history is important for the diagnosis of latex allergy. However, in the presence of a compatible clinical history, the diagnosis of latex allergy should be confirmed by *in vivo* and *in vitro* tests (2–6). Sensitivity and

specificity of the various diagnostic methods are not completely defined both due to differences in allergen sources and due to cross-reactivity with other IgE antibodies, varying still with the risk group under study (7–10).

Latex allergy occurs, in most cases, in people belonging to well-defined risk groups: health care workers, rubber industry workers, children with spina bifida and children subjected to multiple surgical interventions (11, 12). In spite of well identified risk groups, a significant number of

patients who had severe reactions including latex-associated fatal anaphylaxis, did not belong to these risk groups, suggesting that other individuals may be at risk (13).

With the exception of spina bifida patients, latex allergy in children has been less studied than in adults. Various prevalence studies in children not belonging to the surgical risk group have been carried out in several countries, although using different populations (atopic children, non-atopic children, schoolchildren and allergy clinic children; different age groups) as well as different diagnostic methods (questionnaires, skin prick tests and specific IgE). However, the prevalence of latex allergy in children without surgical risk is low, although it seems to be higher in children with previous atopy (14–22).

The possible relationship between latex allergy and food allergy was first described by Leynadier et al. (23). The most frequently implicated foodstuffs are banana, avocado and chestnut. Adverse food reactions in latex allergic children have been described in relation to kiwi fruit, potato, hazelnuts, peach, plum, cherry, watermelon, celery, spinach, tomato, carrot, apple, pear, papaya, oregano, almond, ginger, passion fruit and pineapple (24–26).

Bearing in mind the notion of a growing risk of latex sensitization and allergy also in children, and also in order to gather information about this type of allergy in Portugal, we decided to carry out the present study in atopic and non-atopic Portuguese children.

Materials and methods

Study design

A cross-sectional study was performed with the sample made up of children from the Allergy and the Development outpatient clinics. A non-random, sequential recruitment method was used. A group of 182 children that were at least 3 yr old were recruited: 102 were from the Allergy clinic and 80 from the Development clinic.

Questionnaire

A thorough questionnaire was applied to all children and their relatives. This questionnaire contained questions about household, school or recreational contact with latex-containing products and eventual related adverse reactions. The questionnaire also included questions on food habits (namely regarding foodstuffs implicated in crossreactions with latex) and eventual adverse

reactions upon their ingestion. It also contained questions regarding previous surgical interventions, prolonged medical treatments and the eventual occurrence of allergic or unexplained reactions. Finally, there were also some questions regarding the presence of atopic illnesses and other illnesses affecting the immune system as well as any type of medication.

Skin prick testing

Skin prick tests were performed using allergen extracts in duplicate, on both forearms. A battery containing the most frequent aeroallergens (tree, grass and weed pollens, fungi, cat and dog dander, house dust mites; ALK®) was used. A latex extract at 10 mg/ml was also used (Bial-Aristegui®) (27). Histamine at 10 mg/ml was used as a positive control, and allergen diluent was used as negative control. Reactions equal to or greater than 3 mm were regarded as positive in the presence of a negative control with less than 2 mm in diameter.

Determination of allergen-specific IgE

Blood (5 ml) was taken from all children for the determination of serum total IgE, F × 5E, Phadiatop, latex-specific IgE and food-specific IgE (the latter was determined in children with positive latex-specific IgE and/or skin prick tests).

Quantitation of serum total IgE was performed using an immuno-enzymatic method by direct chemiluminescence; Phadiatop, F × 5E and quantitation of allergen-specific IgE were performed using the Immuno CAP method (Pharmacia, Sweden).

Criteria used for allergy and sensitization to latex

Latex sensitization was diagnosed in the presence of positive latex-specific skin prick tests and/or IgE (≥ 0.35 kU/l). In order to complement the study, an analysis was also performed considering the existence of latex sensitization for values of latex-specific IgE ≥ 0.70 kU/l. *Latex allergy* was diagnosed in the presence of a clinical history suggestive of latex allergy in association with positive latex-specific skin prick tests and/or IgE.

Sensitization to foodstuffs crossreactive with latex was diagnosed in the presence of food-specific IgE ≥ 0.35 kU/l. *Probable food allergy* was diagnosed in the presence of a positive clinical history associated with food-specific IgE ≥ 0.35 kU/l.

Statistical analysis

Absolute and relative frequencies of each variable under study were determined (descriptive statistics).

For the comparison of various parameters between both groups (atopic and non-atopic children), Mann–Whitney *U*-test was used in the presence of non-normal distribution of results, and Student's *t*-test was used in the case of normally distributed data.

Chi-square or Fischer's exact test were used for the comparison of various parameters between the different groups of children with latex sensitization and/or allergy.

A $p < 0.05$ was considered significant.

Results

The age of children studied varied between 3 and 15 yr, without significant differences between both groups (mean age 7.78 yr in the Allergy clinic vs. 7.68 yr in the Development clinic). There were more boys than girls in both groups, but there were no significant differences between the groups from both clinics (Table 1).

Atopy (positive skin prick tests and/or Phadiatop) was detected in 80% of children referred to the Allergy clinic and in 36% of children from the Development clinic, and there was thus a significant difference between these two groups. Prior history of allergic disease was more frequently mentioned by children from the Allergy clinic than from the Development clinic.

There was a broad amplitude of total serum IgE values, with a minimal value of 0 and a maximal value of 2675 kU/l, with a mean of

207.51 kU/l. About 28% of all children had IgE levels ≤ 20 kU/l and 50% had IgE levels ≤ 88 kU/l. Total serum IgE levels were higher in the group of children from the Allergy clinic than in the groups of children from the Development clinic (Table 1).

Accepting latex sensitization in the presence of positive latex-specific skin prick tests and/or IgE, the prevalence of latex sensitization was 20.6% (21/102) in the Allergy clinic, and 6.3% (5/80) in the Development clinic. The total prevalence of latex sensitization was 14.3% (or 9.3%, if we consider IgE ≥ 0.70 IU/ml as positive).

When latex-sensitized and latex non-sensitized children were compared, there were no significant differences in terms of age ($x = 8.53$ vs. $x = 7.67$ yr). Sensitized children had ages between 4 and 12 yr (Table 2).

There were more boys than girls both in the latex sensitized and in the latex non-sensitized groups. A prior history of allergic disease was significantly associated with the presence of latex sensitization ($p < 0.001$; chi-square test).

Total serum IgE levels were higher in latex sensitized than in non-sensitized children ($x = 451.7$ vs. $x = 166.8$), although there was great variability in the levels (minimum of 3 and maximum of 2173 kU/l, in sensitized children). Seventy-three per cent of latex-sensitized children had total IgE levels greater than 176 kU/l, whereas only 26.9% of non-sensitized children had similar values.

All latex-sensitized children were atopic, and there was a significant association between latex

Table 1. Demographic data of patients recruited from the Allergy and Development Clinics

Parameters	Allergy clinic (n = 102)		Development clinic (n = 80)		Total (n = 182)		p-Value (Allergy vs. Development)
	n	%	n	%	n	%	
Age (yr)							
3–6	37	36.2	31	38.8	68	37.4	0.65
7–9	33	32.4	27	33.8	60	33.0	
10–15	32	31.4	22	27.4	54	29.6	
Gender male	59	57.8	47	58.8	106	58.2	0.90
Atopy	81	79.4	29	36.3	110	60.4	
Positive phadiatop	74	72.5	20	25.0	94	51.6	
Positive SPT aeroallergens	77	75.5	26	32.5	103	56.6	<0.001
Allergic disease	75	73.5	8	10.0	83	45.6	
Sensitization to latex (IgE ≥ 0.35 and/or + SPT)	21	20.6	5	6.3	26	14.3	

p-Values were obtained using chi-square test.

Table 2. Demographic data of latex-sensitized and non-sensitized children

Parameters	Sensitized (n = 26)		Non-sensitized (n = 156)		p-Value sensitized vs. non-sensitized
	n	%	n	%	
Age (yr)					
3–6	6	23.0	62	39.7	0.09
7–9	10	38.5	50	32.1	
10–15	10	38.5	44	28.2	
Gender male	16	61.5	90	57.7	0.75
Allergic disease	22	84.6	61	39.1	
Atopy	26	100.0	84	53.8	
Total IgE					
0–26	1	3.8	59	37.8	<0.001
27–175	6	23.1	55	35.3	
176–2675	19	73.1	42	26.9	
Positive phadiatop	24	92.3	70	44.9	<0.001
Positive F $\times$ 5E	16	61.5	41	26.3	
Positive SPT aeroallergens	24	92.3	79	50.6	

p-Values were obtained using chi-square test.

sensitization and atopy ($p < 0.001$; chi-square test) (Table 2).

Of the 26 latex-sensitized children, three had positive latex-specific skin prick tests and IgE, 19 only had positive latex-specific IgE and four only had positive latex-specific skin tests (seven positive skin tests, 22 positive IgE (Table 3).

In children with positive latex-specific IgE ($n = 22$), the values of the latter varied between 0.35 and 21.1, with a mean of 3.03 kU/l.

Thus, depending on the diagnostic method used, the prevalence of latex sensitization varied. If we consider just children with positive latex-specific skin prick tests and/or latex-specific IgE ≥ 0.35 kU/l, the prevalence of latex sensitization was 14.3% but if we consider just children with positive latex-specific skin prick tests, the prevalence of latex sensitization was 3.84% in the total sample; if we take into consideration only children with latex-specific IgE ≥ 0.35 kU/l, the prevalence of latex sensitization was 12.1%. In case we only admit a value of IgE ≥ 0.70 kU/l, the prevalence of latex sensitization would be 6.6% (Table 4).

All latex-sensitized children were atopic, and the prevalence of latex sensitization in atopic children was 23.6%; if we just take into consideration children with only positive latex-specific skin prick tests, the prevalence would be 6.36%,

whereas if we just considered children with only latex-specific IgE ≥ 0.70 KU/l, the prevalence of latex sensitization in atopic children would be 10.9% (Table 4).

There was only one child with a clinical history compatible with latex allergy: he had localized urticaria and conjunctivitis on contact with balloons and rubber balls. This child was a 10-yr-old asthmatic boy, and had a total serum IgE level of 74 kU/l, a positive Phadiatop, a negative F $\times$ 5E, positive skin prick tests to common aeroallergens; a positive skin prick test to latex (7 mm) and a positive latex-specific IgE of 0.57 kU/l, and negative crossreacting food-specific IgE. The prevalence of latex allergy was therefore 0.54% in relation to the total sample of children, and 0.9% in relation to atopic children.

As far as other latex sensitization risk factors are concerned, no child with spina bifida was detected, there was only one child with an urological malformation who had been subjected to multiple surgical interventions, but who was not sensitized to latex. In the sample studied, there was no significant association between the number of surgical interventions and atopy, or latex sensitization.

Of the 26 latex-sensitized children, 16 (61.5%) had elevated levels (≥ 0.35 kU/l) of IgE specific to at least one of the foodstuffs crossreacting with latex. Of the 26 latex-sensitized children, 21 were also sensitized to grass pollens (positive skin prick tests). In these children, there was a trend for a positive association between sensitization to latex cross-reacting foodstuffs and grass pollens ($p = 0.055$; Fischer's exact test) (Table 5).

All children with positive IgE to latex-crossreacting foodstuffs also had positive latex-specific IgE (Table 6). All four latex-sensitized children that only had latex-specific skin prick tests but not latex-specific IgE, had negative foodstuff IgE. The only child with latex allergy had a negative IgE specific to latex crossreacting foodstuffs. Only one child had a possible food allergy, with a history of vomiting upon the ingestion of watermelon and watermelon-specific IgE of 0.73 KU/l.

Table 3. Values of latex sensitization, as determined using various diagnostic methods in all children under study

	Positive SPT to latex	Negative SPT to latex	Total
Latex-specific IgE ≥ 0.35	3	19	22
Latex-specific IgE < 0.35	4	156	160
Total	7	175	182

Table 4. Prevalence of latex sensitization and allergy in children from the Allergy and the Development clinics, according to the various diagnostic methods used

	Group							
	Allergy (n = 102)		Devel- opment (n = 80)		Atopic (n = 110)		Total (n = 182)	
	n	%	n	%	n	%	n	%
Latex-specific tests								
Positive SPT and/or specific IgE ≥ 0.35	21	20.6	5	6.3	26	23.6	26	14.3
Positive SPT and/or specific IgE ≥ 0.70	14	13.7	3	3.8	17	15.5	17	9.3
Positive SPT	5	4.9	2	2.5	7	6.4	7	3.8
Specific IgE ≥ 0.35	19	18.6	3	3.8	22	20.0	22	12.1
Specific IgE ≥ 0.70	11	10.8	1	1.3	12	10.9	12	6.6

Table 5. Prevalence of sensitization to latex-crossreacting foodstuffs and grass pollen allergens in latex-sensitized children

	Latex-crossreacting foodstuff specific IgE ≥ 0.35		
	Yes	No	Total
Sensitization to grass pollens (+SPT)			
Yes	15	6	21
No	1	4	5
Total	16	10	26

$p = 0.055$ (Fisher's exact test).

Table 6. Prevalence of sensitization to latex-crossreacting foodstuffs in relation to latex sensitization, as determined by various methods in latex-sensitized children

	Sensitization to latex			Total
	Specific IgE ≥ 0.35	Positive SPT and specific IgE ≥ 0.35	Positive SPT	
Sensitization to latex-crossreacting foodstuffs (specific IgE ≥ 0.35)				
Yes	14	2	0	16
No	5	1	4	10
Total	19	3	4	26

The most prevalent sensitizations to latex crossreacting foodstuffs were tomato, papaya, avocado, banana, watermelon and apple.

Discussion

The present study aimed at characterizing the prevalence of latex allergy and sensitization in a Portuguese paediatric population. It therefore included a sample of children from two different hospital clinics – a Development clinic, representative of the general population, and an Allergy clinic, representative of a specialty clinic. Both groups had similar features in terms of age, sex, systemic illnesses and number of previous surgical interventions, but were different in terms of the presence of atopy and allergic disease, with obviously more allergic children in the group from the Allergy clinic. In total, we found 26 children sensitized to latex, and the prevalence of sensitization was 20.6% in the Allergy group and 6.3% in the Development group.

All latex-sensitized children were atopic, 23.6% of atopic children were sensitized to latex, and 0.9% of atopic children had latex allergy. In contrast, in non-atopic children, latex sensitization was 0.0%. Latex-sensitized children had more elevated total serum IgE levels.

Of the 26 latex-sensitized children, 16 were simultaneously sensitized to one or more latex-crossreacting foodstuffs (61.5%). Twenty-one children were simultaneously sensitized to latex and grass pollens; 15 children were sensitized to latex, food and grass pollens.

Given the great variability in the prevalence values of latex sensitization found in different studies, which was probably due to varying population sampling methods and populations, as well as diagnostic approaches, we included in our study the three principal diagnostic methods for latex sensitization/allergy: clinical history, skin prick tests and quantification of latex-specific IgE, which were performed systematically in all children, independently of a history of

latex allergy. As far as we know, only one previously published study used the same approach, although in a different population of children (22). Data obtained using our approach contribute towards a more comprehensive analysis of latex sensitization, thereby allowing comparison of our results with those from other previous studies.

In order to be able to compare our results with those from other groups, we decided to analyse the data for latex-specific IgE levels considering both 0.35 and 0.70 kU/l as cut-off levels for positivity. In fact, in terms of latex allergy in children, studies are scarce.

The characterization of sensitization to latex cross-reacting foodstuffs in latex-sensitized children, has been hardly analysed in previous studies, and allows us to have an idea of the foodstuffs most frequently implicated in such crossreactivity in Portuguese children.

In our sample, the prevalence of latex sensitization was 20.6% in the Allergy clinic group, and 6.3% in the Development clinic group. Thus, as expected, the prevalence of latex sensitization was higher in children referred to an allergy specialist clinic than in children referred to a routine developmental clinic, which is more representative of the general paediatric population. When children from both clinics were analysed as a whole, the prevalence of latex sensitization was higher in atopic than in non-atopic children (23.6% vs. 0.0%, respectively). Such prevalence values are somewhat higher than those observed by other groups. However, in the present study, both skin prick tests and determination of latex-specific IgE were performed in all children, which significantly increases the detection capacity of sensitized children, particularly because skin prick tests and specific IgE were only concordant in three children. On the other hand, there were more children with positive specific IgE than with positive skin prick tests, which is in agreement with the results found by other groups. For instance, Jensen et al. (22) studied latex sensitization in 100 atopic children from an Allergy clinic, using skin prick tests and latex-specific IgE; 5% of the children had positive skin prick tests, 4% of the children had positive latex-specific IgE. Ninety-nine per cent of the children had symptoms of allergic disease (which is higher than the figure observed in our study) and a value of 0.70 kU/l was used as a cut-off level for specific IgE positivity. Accepting such cut-off values for our study, the prevalence of latex sensitization in atopic children was 15.4%. In another study, Cremer et al. (28) compared latex sensitization between children

with spina bifida and atopic children and observed a prevalence of 11.4% in the latter group, for a cut-off level of latex-specific IgE of 0.70 kU/l.

The results obtained in the present study may also be compared with those from other groups. Thus, in another study, Bernardini et al. studied 1175 schoolchildren (general paediatric population), basing his diagnosis of latex sensitivity exclusively on skin prick test results; a prevalence of latex sensitization of 0.7% was found (19). In our study, and just accepting as a diagnostic criterion positive skin prick tests in children from the Development clinic (also representative of a general paediatric population), the prevalence of latex sensitization was 2.5%. In fact, 36.2% of the children from this clinic were atopic, a value identical to that found by Bernardini in schoolchildren, which further strengthens the idea that the children from the Development clinic are just as representative of the prevalence of latex sensitization in a general paediatric population as is the case of schoolchildren.

The presence of atopy was, in the present study, a highly significant risk factor as latex sensitization in atopic children was 23.6% whereas it was 0.0% in non-atopic children. This is in agreement with the results obtained in other studies involving children without surgical risk and which demonstrated a significantly higher prevalence of latex sensitization in atopic than in non-atopic children, independently of the latex diagnostic methodology utilized. For instance, Shield and Blaiss (14) found a prevalence of 6.8% in atopic children and a prevalence of 0.0% in non-atopic children; Danne et al. found a prevalence of latex sensitization of 26.0% in atopic and 0.0% in non-atopic children (26). Finally, Liebke et al. found a prevalence of latex sensitization of 20.8% in atopic children and of 0.3% in non-atopic children (18). In the latter study, Liebke et al. (18) compared between atopic ($n = 306$) and non-atopic ($n = 303$) children using as a diagnostic criterion specific IgE levels ≥ 0.35 kU/l whereas in Shield and Blaiss study (14) using latex glove extracts, 3/44 atopic children had positive SPT.

Akasawa et al. (15) found latex-specific IgE in 10.2% atopic children (11/108) with total serum IgE higher than 1000 kU/l and in 0.5% (1/196) of children with total serum IgE of less than 1000 kU/l. In this study, a concordance between latex-specific skin prick tests and IgE was found in 7 out of 12 sensitized children whereas in the present study only 3 out of 22 children with positive specific IgE also had positive skin prick tests to latex. This may, in part, depend on the

latex extracts used. For the current study, we used a skin prick test latex extract that has previously been shown to have good specificity and sensitivity (27), although it showed to be less sensitive than we initially thought.

In the present study, and accepting as latex sensitized only children with positive skin prick tests but not specific IgE, the prevalence of latex sensitization was 4.9% in the group from the Allergy clinic, which is higher than the value observed by Ylitalo et al. (17) in a group of children admitted to a hospital clinic for allergy skin testing, using the same diagnostic method (1.9%). In another study, by Novembre et al. (20), the prevalence of latex sensitization based on positive skin prick tests was 3%.

With the exclusion of studies involving children with surgical risks, the prevalence of actual latex allergy has been low in previous studies: Jensen et al. – 1%; Novembre et al. – 1.5%; Liebke et al. – 2.9%; Shield et al. – 0.0%; Ylitalo et al. – 1.0%; in our study, it was 0.0% in non-atopic children and 0.99% in atopic children. In atopic children, there seems to be a higher concordance between positive latex-specific skin prick tests and IgE: both in the present work and in that of Jensen et al. there was a child with clinical symptoms of latex allergy and a positive latex-specific skin prick test. Latex-specific IgE in the child in our study was 0.57 kU/l, which raises some doubts as to using 0.70 kU/l as a cut-off level for positive latex-specific IgE. In the study by Novembre et al., 5 out of 10 children with a positive skin prick test to latex had clinical symptoms of latex allergy and only one had negative latex-specific IgE. Thus, although we cannot reach a conclusion about the best diagnostic method for latex sensitization or allergy, most studies point towards a concordance between both tests in children with actual latex allergy.

In the present study, latex-sensitized children had significantly higher total IgE values than non-sensitized children. Since studies of the relationship between IgE levels and latex sensitization are scarce and involve relatively few patients (16, 17, 22), future studies involving larger samples should be performed.

As far as sensitization to foodstuffs is concerned 16 out of 26 latex-sensitized children were simultaneously sensitized to one or more latex-crossreacting foodstuffs, which corresponded to a frequency of co-sensitization of 61.5%. In the study by Novembre et al. (20), the most frequently implicated foodstuffs were kiwi fruit, chestnut and apple. Ylitalo et al. studied the prevalence of sensitization to banana, kiwi fruit

and avocado using skin prick tests with fresh fruit and observed that the three fruits were implicated in the sensitization although more frequently in children without surgical risk. In the study by Pires et al. (29) in children with spina bifida, 23.5% of latex-sensitized children were also predominantly sensitized to banana, pineapple and potato.

There is thus a great variation in the prevalence of sensitization to foodstuffs in the various studies, particularly when children with and without surgical risk are compared. Therefore, more studies with larger samples and using standardized latex and food extracts should be carried out.

In summary, in the present study, the prevalence of latex sensitization in children referred to hospital clinic was 20.6% in the group from the Allergy clinic, and 6.3% in the group from the Development clinic. The prevalence of sensitization was 23.6% in atopic children, and 0.0% in non-atopic children. The prevalence of latex allergy was 1% in atopic children. Latex sensitization was therefore highly correlated with atopy.

About 62% of latex-sensitized children were simultaneously sensitized to latex-crossreacting foodstuffs.

Previous allergic disease, positive Phadiatop, positive skin prick tests to common aeroallergens, elevated total serum IgE were significantly associated with sensitization to latex. The number of previous surgical interventions was not a risk factor for sensitization to latex.

It will be important to follow up this group of latex-sensitized children over a period of a few years in order assess the natural history of sensitization and to determine whether these children ever actually developed clinical latex allergy when exposed to latex or rubberized materials in every day life.

This study shows that the prevalence of latex allergy and sensitization in Portuguese atopic and non-atopic children without surgical risks, as analysed using various diagnostic methods, is similar to that observed in other countries. In addition, the assessment of latex allergy and sensitization should always include both skin prick testing and determination of serum IgE.

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