
Latex sensitization in children with spina bifida: follow-up comparative study after two years

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Background: Previous findings suggest that sensitization to latex in children with spina bifida is a dynamic process.

Objective: To study if changes appear in the sensitization status after withdrawal of latex.

Methods: We studied a consecutive sample of 68 children with spina bifida, by means of latex skin prick tests and quantification of serum latex-specific IgE on two separate occasions two years apart.

Results: Forty-four (65%) were classified as nonsensitized, 6 (9%) showed indeterminate results, and 18 (26%) were sensitized to latex, six of whom had clinical reactions to latex. They were instructed to avoid latex. In a second evaluation, 2 years later, 38 (56%) were classified as nonsensitized, 3 (4%) as indeterminate, and 27 (40%) as sensitized to latex, 11 of whom had presented latex symptoms. This meant 22% of spina bifida children demonstrated progressive sensitization, in spite of having adopted a latex-free environment at our hospital. It illustrates the progressive character of latex sensitization in these patients.

Conclusion: Latex avoidance measures both in the medical and home settings must be stressed. We recommend that children with spina bifida should be periodically evaluated regarding latex sensitization.

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INTRODUCTION

The spectrum of latex-related allergic reactions ranges from mild urticaria, to rhinitis, bronchospasm, and anaphylactic reactions, which can cause death.^{1–4} Diagnostic awareness, greater exposure to latex products, and changes in the manufacturing of latex have been proposed as causes of the increasing frequency of reports on latex hypersensitivity in health care workers and other high risk groups, such as children with spina bifida.⁵ Among these, prevalence of sensitization to latex has been described in up to 80%.^{4,6–14} The main risk factors identified thus far include the number of prior surgical procedures and atopy.^{6–9,11,14} In a first evaluation,¹⁴ we classified our patients

with spina bifida in four groups, on the basis of skin tests and serum-specific IgE results. There were two groups with clearly positive results of sensitization to latex, one of these groups presenting clinical symptoms to latex. A third group comprised nonsensitized patients with negative results in the tests. The fourth group included some patients with indeterminate results, who had intermediate results both in diagnostic tests and in risk factors. They were suspected to be in the early stages of sensitization, with so low, but not absent, levels of latex-specific IgE that they could not be definitely included in the other groups. The aim of the present work was to study and compare the sensitization status in a cohort of children with spina bifida, 2 years after recommending avoidance of latex and having adopted a latex-free environment in our hospital, to watch if changes occur, which highlight the natural history of latex allergy.

PATIENTS AND METHODS

In 1994 we started the systematic study of all children with spina bifida followed since birth in the outpatient clinic of the Pediatric Urology Section of a tertiary reference center. They were investigated about clinical reactions to latex, which included urticaria, edema of face and lips, tongue itching, rhinitis or cough, with balloons, gloves, cholonostomy bags and other devices, and an anaphylactic reaction in one patient while undergoing a cystourethrogram. Data were gathered about risk factors for latex sensitization, which included the number of operations, the levels of serum total IgE, the presence of a ventricular-peritoneal shunt, and a personal history of atopy. This was considered positive if there existed a history of asthma, rhinitis, conjunctivitis, atopic dermatitis or urticaria not related to latex.

In Vivo Tests

After informed consent was obtained from parents, skin prick tests with commercial latex antigen (ALK-Abello Labs, Spain) were done in all the patients. As described previously,¹⁴ skin tests were graded 0 to 4+ compared with 1% glycerinated histamine, according to a method similar to that of Turjanmaa.¹⁵ No wheal was graded as 0+, wheals with an area up to 25% of the wheal elicited by histamine were graded as 1+, 2+ when the area was between 25% and 50%, 3+ when the area was between 50% and 75%, and 4+ when it exceeded 75%. No wheals were observed with saline solution control tests. Skin tests caused no adverse reactions.

In Vitro Tests

Serum latex-specific IgE (Pharmacia CAP System RAST FEIA, Uppsala,

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Sweden) was measured in all cases, and graded, as suggested by the manufacturer, as class 0 for values lower than 0.35 U/mL, class 1 for values between 0.35 and 0.7, class 2 between 0.7 and 3.5, class 3 between 3.5 and 17.5, class 4 between 17.5 and 50, class 5 between 50 and 100, and class 6 for values greater than 100 U/mL.

Classification of Patients

Patients were classified according to responses to both "in vivo" and "in vitro" tests. Patients with strong responses (skin test >2+ and CAP class >2) in any of the tests were considered to be sensitized to latex. One patient with a skin test of 2+ and latex-specific IgE of class 2, concordant with each other, was also classified as sensitized. Patients with both tests negative, or with only one of them with a very weak response (skin test 1+, CAP class 1) were classified as non-sensitized. The rest (patients with responses 0 and 2, 1 and 1, and 1 and 2 in the tests) were considered to have indeterminate results.

All patients were thereafter treated in a latex-free environment¹⁶ in our hospital, and they were also given written instructions to avoid contact with products containing latex, eg, balloons, toys, bottle nipples, pacifiers, rubber bands, kitchen gloves, etc, and to warn medical personnel not to use latex gloves if care was provided elsewhere.

A consecutive sample of 68 of these children with spina bifida was re-evaluated 2 years later, using the same diagnostic commercial methods and the same classification criteria. They were questioned again about the presence of clinical reactions to latex not previously experienced, and reclassified in the diagnostic groups described above.

Patients with positive results in tests but without a history of latex reactions underwent a "use test." They put on a latex glove fingertip, and if no reaction was found after 10 minutes, they put on a latex glove in one hand, and a latex-free glove in the other. They were examined for clinical reactions as rash, itching, urticaria, rhinitis, or cough.

RESULTS

We studied a consecutive sample of 68 children with spina bifida (33 male). The mean (SD) age at the first evaluation in 1994 was 7.2 (4.5) years and 9 (4.5) years at the second evaluation in 1996. Following the aforementioned criteria, in the first evaluation 18 (26%) patients were considered to be sensitized to latex, 6 of whom had presented clinical symptoms related to latex; 44 (65%) were not sensitized, and in 6 cases (9%) results were indeterminate.

In the second evaluation, using the same reagents, the cutaneous response had increased in 18 children, decreased

in 3, and remained the same in 47. Changes in the level of serum latex-specific IgE were found in half of the patients. Specific IgE was considered to have changed if there was a decrease or an increase beyond the coefficient of variation between assays of the technique, which is 6% to 9% according to the manufacturer. Decreases were lower than increases, as shown in Table 1. With the combined use of skin and CAP tests of the second evaluation, 27 (40%) children were classified as sensitized, 11 of whom were latex symptomatic, 38 (56%) were not sensitized, and 3 (4%) were indeterminate. Thus 22% of the patients ascended in the sensitization classification, 4% descended, and 74% remained in the same group. The evolution of sensitization status of all patients is shown in Table 2. In Table 3 we show the results of skin and CAP tests of the 18 patients whose sensitization status changed in the second evaluation. The use test was performed in the 16 patients with positive test results but without clinical symptoms, and no reactions were found.

In each classification group, comparisons were made between patients who had ascended in their sensitization status, and those who had not. The results on number of operations, serum total IgE, personal history of atopy and presence of a ventricular-peritoneal shunt failed to show distinct differences, although the small number of patients in each group precludes definitive conclusions.

DISCUSSION

Latex allergy is frequent in multioperated children, especially in those with spina bifida.⁶⁻¹⁴ The repeated exposure to amounts of latex antigens through multiple diagnostic and therapeutic procedures, beginning in the first day of life, seems to be responsible for the high frequency of latex allergy.^{7,8,14} There is a statistical association of the number of operations and other factors, as the atopic diathesis, with the presence of latex sensitization in children with spina bifida.^{6,7,9,12} In previous studies we have demonstrated that

Table 1. Increases and Decreases in the Level of Serum Latex-Specific IgE Between the First and the Second Evaluation

	Increase	Decrease
No. of patients	18	14
Age (mean $\pm$ SD)	9.3 $\pm$ 4.6	10.8 $\pm$ 3.8
IgE change (mean $\pm$ SD) kU/L	7.1 $\pm$ 12.3	2.9 $\pm$ 3.8
IgE change range kU/L	0.08 – 52.6	0.09 – 10.5
IgE change <0.5 kU/L	3 / 18	6 / 14
IgE change 0.5–1 kU/L	0 / 18	2 / 14
IgE change >1 kU/L	15 / 18	6 / 14
RAST class change	15	9
1 RAST class change	7	8
2 RAST classes change	5	1
3 RAST classes change	3	0

* No change was found in the other 36 patients.

Table 2. Number of Patients in Each Classification Group in First and Second Evaluations

1994 Evaluation		1996 Evaluation			
	No. of Patients	NS 38	ID 3	SA 16	SS 11
NS*	44	36	2	5	1
ID	6	2	0	3	1
SA	12	0	1	8	3
SS	6	0	0	0	6

* NS = nonsensitized, SA = sensitized asymptomatic, ID = indeterminate, and SS = sensitized symptomatic.

there is a gradual increase in serum latex-specific IgE levels from nonsensitized children to indeterminate patients, following to asymptomatic and finally symptomatic sensitized children.¹⁴ This had been found in a cross-sectional study, suggesting that there is a dynamic process of sensitization, with detectable latex-specific IgE slowly raising in response to subsequent exposures to latex, as children undergo more operations and latex antigens have a direct contact with blood vessels and open mucosas.

In the present study, we have studied a group of children with spina bifida on two separate occasions. We have thus confirmed our previous impressions about the dynamic character of latex sensitization. In 15 patients (22%) of those studied, there has been a rise in sensitization classification, while only in 3 cases (4%) there has been a fall: two indeterminate patients down to the nonsensitized group, and one sensitized asymptomatic child to the indeterminate group.

Different allergen reagent sources may be used for the study of latex sensitization,¹⁷ and diagnostic criteria vary among the published studies.⁶⁻¹⁴ We employed commercial extracts and, to avoid false positive results, our criteria were more strict, especially for RAST, than those used in most previous studies.⁶⁻¹³ Consequently, patients that might have otherwise been classified as sensitized, were classified as indeterminate in our study. After analysis of the diagnostic value of tests, we have proposed other alternative criteria (manuscript submitted). In the present report, we have used the original diagnostic cut/off points,¹⁴ but we made a

parallel analysis, using the new criteria in both evaluations, basically 2+ in skin tests and CAP class ≥ 2 as diagnostic value for sensitization, and results were practically identical, with 16 patients ascending and one patient descending in the sensitization classification. The use of different classification criteria would seem to yield the same general findings.

Before our first evaluation, children in our hospital were treated with gloves and medical material containing latex. We started to manage spina bifida children in a latex-free environment after that, and patients were instructed to avoid latex in their homes. Despite this, in the second evaluation after 2 years of avoidance, latex sensitization was more frequent. Once initiated, the process of sensitization will not stop in this period of time, but will proceed in a high proportion of patients. This fact, in spite of latex avoidance measures, should be a cause of concern. Exposure to apparent or inapparent sources of latex in household products not only cannot be ruled out, but it can be ascertained since several patients declare to present symptoms not previously shown, meaning they had had contact with latex. A potential role of cutaneous contact with latex in the progress of latex sensitization, in children previously exposed through blood vessels and open mucosas, might be involved. Our patients were not exposed to direct contact with latex, but airborne particles of latex in shared hospital rooms, where other patients had been treated with latex products, might be inhaled by them, causing a repeated antigenic stimulus. Other explanations should also be considered, such as a role for cross-reactive foods inducing or maintaining latex sensitization, or the presence of reservoirs of latex in tissues from preceding operations causing a slow release and antigenic stimulation by latex. Regarding this, ventricular-peritoneal shunts implanted in our patients were made of silicone, with no latex, but prior to their installation they were revised by a surgeon wearing latex gloves, and none of the six patients

Table 3. Results of Skin and Latex CAP Tests in the 18 Patients Whose Sensitization Status Changed in the Second Evaluation

Sensitization Status		Skin Prick Test		RAST kU/L (Class)	
1994	1996	1994	1996	1994	1996
NS	ID	0	1	<0.35 (0)	0.83 (2)
NS	ID	1	0	<0.35 (0)	1.9 (2)
NS	SA	0	4	<0.35 (0)	4.89 (3)
NS	SA	0	4	<0.35 (0)	2.57 (2)
NS	SA	0	4	<0.35 (0)	4.94 (3)
NS	SA	0	4	0.42 (1)	0.41 (1)
NS	SA	0	3	<0.35 (0)	5.61 (3)
NS	SS	0	2	<0.35 (0)	2.92 (2)
ID	NS	1	0	0.55 (1)	<0.35 (0)
ID	NS	0	0	2.02 (2)	<0.35 (0)
ID	SA	0	4	1.26 (2)	0.38 (1)
ID	SA	2	4	0.36 (1)	0.51 (1)
ID	SA	0	4	1 (2)	7.04 (3)
ID	SS	1	4	0.48 (1)	8.28 (3)
SA	ID	4	2	<0.35 (0)	<0.35 (0)
SA	SS	3	4	4.52 (3)	9.57 (3)
SA	SS	4	4	10.2 (3)	7.06 (3)
SA	SS	4	4	38.8 (4)	91.4 (5)

* NS = nonsensitized, SA = sensitized asymptomatic, ID = indeterminate, and SS = sensitized symptomatic.

without a shunt changed their sensitization status (all of them with CAP <0.35 and 0+ in skin tests on both evaluations). The role of this device remains controversial,¹⁸ but in our previous report, using a multivariate study, it was identified as synergistic, with additional information to that of the number of operations.¹⁴ Our present data indicate the progressive character of latex sensitization in children with spina bifida in spite of latex avoiding measures, but they neither prove nor disprove these or other hypotheses.

A recent study in this same subject has been published by Cremer et al.¹⁹ They show an increase of latex-specific IgE levels in 12/67 children, and a decrease in 18/67, but only three of these might be considered to have changed their sensitization status (2.3, 1.3, and 0.7 U/mL down to <0.35, 0.4 and <0.35 U/mL respectively), so their results do not differ much from ours. Reports in sensitized healthcare workers show a slow decrease in skin reactivity and serum-specific IgE, but not its disappearance, after a period of 6 to 18 months of latex avoidance.^{20,21} In our patients, the ratio of increases to decreases was 5:1, and these were of smaller magnitude than the increases of both skin and CAP tests responses.

Recommendations for the management of spina bifida children include a latex-free environment for medical and surgical procedures since birth.¹⁶ The development of latex products free of the offending antigens, the use of latex immunotherapy,³ or the use of alternative sources of natural rubber²² are trends for the future. Currently, we recommend that more stress must be put on the avoidance of latex both in and out of the medical setting, and that all children with spina bifida be investigated about latex allergy and periodically re-evaluated.

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