

Risk factors for latex allergy in patients with spina bifida

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Summary

Objective and methods In order to study risk factors for latex allergy in patients with spina bifida, we investigated 165 patients with spina bifida (mean age 9 years). Besides answering a questionnaire, patients underwent skin-prick testing and determination of specific serum IgE to latex as well as a screening test for specific IgE to environmental allergens. A total of 80 patients (49%) were sensitized to latex according to the presence of specific IgE to latex.

Results Skin-prick tests (SPT) with high ammonia latex milk were performed in 81 of our patients with spina bifida and were positive in 36 patients (46%). Concordance of SPT with specific IgE in serum was good. Nineteen out of 165 patients suffered from a clinically relevant latex allergy: five patients had a history of systemic reactions to latex (e.g. severe bronchospasm, anaphylactic reactions), mostly during surgery. Fourteen patients reported clinical symptoms while inflating a balloon; all these 19 patients were sensitized to latex. Number of operations ranged from one to 26 (mean 5 operations). Concentration of specific IgE to latex in serum correlated well with increasing numbers of operations. Some 32/76 patients (41%) with spina bifida who were sensitized to latex showed an atopic disposition, while 21 out of 81 latex-negative patients (26%) were atopic. Of 300 consecutive sera (mean age of patients 9 years) sent to our laboratory for routine determination of specific IgE, 144 (48%) were positive in terms of specific IgE to environmental allergens, of which 24/144 (17%) were sensitized to latex.

Conclusions From our data we conclude that in order to minimize risk of severe systemic clinical reactions, all patients with spina bifida should be screened for their individual risk of latex allergy to plan preventive measures before operations. Main risk factors for latex allergy seem to be: more than five operations, atopic predisposition, history of clinical symptoms while inflating a balloon, and a sensitization with a CAP-class of ≥ 4 .

Keywords: allergy, latex, spina bifida

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Introduction

Allergens from natural rubber latex (NRL) are widely distributed in indoor conditions. One important factor is the increased use of gloves containing latex. While delayed type hyperreactivity reactions are well known,

there have been an increasing number of reports on immediate type reactions in recent years: symptoms are often severe, including full anaphylaxis [1–5]. Sensitization rates to latex differ in various populations and seem to be high in extensionally exposed persons. It is not sure whether exposure or a predisposition is the main factor for sensitization, or both together.

Due to their very early and extensive exposure, children with spina bifida are especially prone to sensitization to latex. Recently, a 27 kDa NRL protein from

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latex-allergic children with spina bifida was characterized which is associated with clinical manifestations of latex allergy [6].

Because of anaphylactic reactions of some of our children during surgery, we investigated a large number of spina bifida patients in order to detect possible risk factors for sensitization and allergy to latex.

Materials and methods

Patients and controls

We investigated 165 patients with spina bifida (81 females, 84 males). Ages ranged from 9 months to 52 years (mean age 9 years). In addition, sera from 300 children without spina bifida (mean age 9 years) which were sent to our allergy laboratory for routine determination of IgE were also investigated for specific IgE to latex.

Study design

In this cross-sectional study, all out-patients with spina bifida from our Division of Neuropaediatrics were recruited. A questionnaire was handed over to them; 159 patients (96%) or relatives returned their questionnaires. Questions covered history, number of operations, contact with latex and atopic diseases. At the same time-point, skin-prick tests (SPT) were performed and blood was taken.

Methods

Total IgE, specific IgE to latex and a screening test for environmental allergens (SX1) were determined in 163 patients using a solid-phase immunoassay (FEIA), the Pharmacia CAP-system (PCS) (Kabi-Pharmacia, Uppsala, Sweden) [7]. Results of specific IgE to latex are expressed in kU/L and/or in CAP-classes.

SPT was performed with high-ammonia natural rubber latex milk (Ansell, Munich, Germany). The result was assessed as positive, if the weal was ≥ 3 mm without reaction of negative control. SPT-data are given for 81 patients of our total study population, because we first used a SPT with a commercial extract with completely insufficient sensitivity.

For statistical analysis, unpaired *t*-test and Mann-Whitney *U*-test were used.

Results

Sensitization to latex

Serum could be obtained from 163 patients. According

to the presence of specific IgE in serum, 80 patients with spina bifida (49%) were sensitized to latex (CAP-class ≥ 1). Concentration of specific IgE in the 80 sensitized patients ranged from 0.36 kU/L (CAP-class 1) to > 100.0 kU/L (CAP-class 6). Sensitization followed a nearly normal distribution in our patients (Fig. 1).

SPT with high ammonia latex milk was positive in 37/81 patients with spina bifida (46%). No appreciable side-effects of SPT were noted. Concordance of SPT with specific IgE in serum was good: nine patients (11%) were SPT negative, but had specific IgE to latex in serum, while only one child was SPT-positive, but showed no specific IgE to latex (Table 1). Sex ratio in sensitized patients did not differ significantly from non-sensitized patients.

Clinically relevant allergy to latex

Five children (3%) had a clear history of systemic reactions to latex – four of them peri-operatively. Symptoms included severe bronchospasm, anaphylactic reactions and generalized urticaria (Table 2). Diagnoses of these symptoms were based on reports of physicians responsible for these patients. Mean specific IgE was 49.1 kU/L (CAP-class 4), mean age 10.2 years. Patients with systemic clinical reactions had been operated on an average of nine times. Four of these patients also reported local symptoms while inflating a balloon.

Fourteen out of 165 patients (8.5%) reported clinical symptoms while inflating a balloon (Table 3). Mean age was 9 years. All these patients were sensitized to latex: mean specific IgE in this group was 49.7 kU/L (CAP-class 4).

Specific IgE to latex was significantly higher

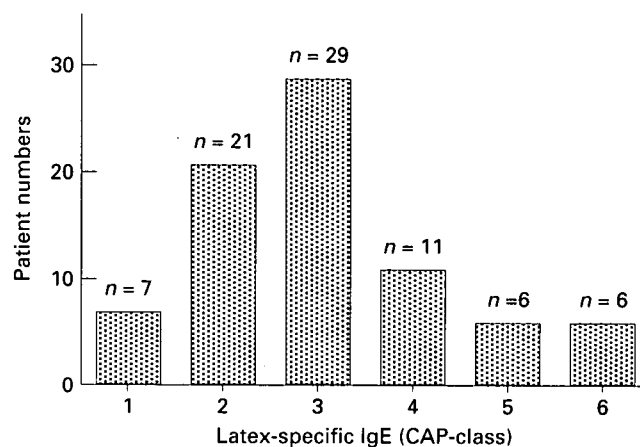


Fig. 1. Distribution of specific IgE to latex in patients with spina bifida ($n = 80$).

Table 1. Concordance of specific IgE against latex in serum and SPT with natural latex milk

	Specific IgE latex positive	Specific IgE latex negative	
SPT positive	36 (97%) (80%)	1 (3%) (3%)	37
SPT negative	9 (20%) (20%)	35 (80%) (97%)	44
	45	36	81

($P < 0.004$) in the group of symptomatic ($n = 15$) patients compared with the group of non-symptomatic ($n = 65$) patients (Fig. 2).

Number of operations

The number of operations in the spina bifida group ranged from 1 to 26 (mean five operations). Every patient underwent surgery on the first day of life.

Concentration of specific IgE to latex in serum correlated with increasing numbers of operations and was statistically significant from CAP-class 3 on (Fig. 3). Patients with (systemic or local) symptoms had been operated on significantly more often than sensitized patients without clinical symptoms ($P < 0.0004$) (Fig. 4). Sensitized patients without symptoms had undergone significantly more surgery than non-sensitized patients ($P < 0.004$) (Fig. 4).

Table 2. Data of five patients with severe systemic reactions

Initials	Sex	Age (years)	Total IgE (kU/L)	Atopy yes/no	Specific-IgE latex (kU/L)	Clinical symptoms	Occasion of symptoms	Number of operations
B.S.	F	7.7	17	No	41.0	OBS, cyanosis, conjunctivitis, SL	At home by airborne glove powder	3
M.T.	M	5.8	80	No	6.7	OBS, cyanosis	Post-OP	6
K.M.	M	13.3	263	No	74.3	OBS, cyanosis	Post-OP	17
S.R.	M	6.8	157	Yes	11.8	OBS, cyanosis, art. hypotension	During OP	11
H.S.	M	8.3	43	Yes	11.5	Conjunctivitis, SL, URT	During OP	7
Mean		10.2						9

OBS. Severe bronchospasm. SL. Swelling of lips. URT. Generalized urticaria.

Atopic disposition

Thirty-two out of 76 patients (42%) with spina bifida who were sensitized to latex showed an atopic disposition (based on positive specific IgE to environmental allergens = positive SX1), while 21 out of 81 latex-negative patients (26%) were atopic.

Control group

Of 300 sera sent to our laboratory for routine determination of specific IgE 144 (48%) were positive in terms of specific IgE to environmental allergens (= atopic patients). Of these 144 atopic patients, 24 (17%) were sensitized to latex. Only one out of 156 non-atopic patients showed an isolated sensitization to latex (CAP-class 4) without specific IgE to common environmental allergens. This patient reported typical clinical symptoms while inflating a balloon.

Discussion

Sensitization to latex

We found a rate of sensitization to latex of 49% in the spina bifida group. In the literature, prevalence rates range from 34% [8], 40% [9] and 49% [10] up to 64.5% [11]. The validity of our data may be high, because we investigated the largest number of spina bifida patients published so far.

Hypotheses for the high prevalence of sensitization to latex in patients with spina bifida include extensive contact of gloves containing latex on large mucosa areas during multiple surgery very early in life [12];

Table 3. Data of 14 patients with clinical symptoms while inflating a balloon

Initials	Sex (f/m)	Age (years)	Total IgE (kU/L)	Atopy yes/no	Specific IgE latex (kU/L)	Number of operations	Local symptoms
B.S.	F	7.7	166	No	41.0	3	SL, CJ
K.K.	F	4.5	28	No	2.7	8	SL, itching
D.L.	M	5.5	1170	Yes	81.1	6	URT
M.T.	M	5.8	98	No	6.7	5	SL
G.S.	M	6.2	1430	Yes	> 100.0	4	SL, itching
D.M.	F	6.4	149	No	99.7	6	CJ
S.R.	M	6.8	157	Yes	11.8	11	SL
R.T.	M	7.7	329	Yes	> 100.0	12	SL
H.S.	M	8.3	42	Yes	11.5	7	CJ
B.M.	F	12.3	196	Yes	11.1	7	SL
P.J.	M	12.6	68	No	2.3	10	SL, itching
S.T.	F	17.6	613	Yes	> 100.0	20	SL
S.S.	F	6.7	157	Yes	11.8	11	SL, itching
B.M.	M	14.2	158	No	32.3	21	SL
Mean		8.8				9	

SL. Swelling of lips. URT. Facial urticaria. CJ. Conjunctivitis.

perpetual contact by urinary catheters containing latex; and daily contact with latex gloves used for routine care.

Determination of specific IgE with the CAP-system seems to be a more sensitive measure than SPT in our setting, although concordance in our patients was good. The lower number of positive SPT in comparison to serum IgE may be explained by the latex material used for skin test. Unfortunately, an identical latex source for

in vitro and *in vivo* testing is not available so far. Choosing the extract for skin-prick testing (SPT) is the crucial point of *in vivo* tests; we therefore took a natural rubber latex milk which is known to be the most sensitive extract for SPT.

SPT-data are given for about 50% of our total study population, because for the first tests we used a commercial extract which proved to have completely insufficient

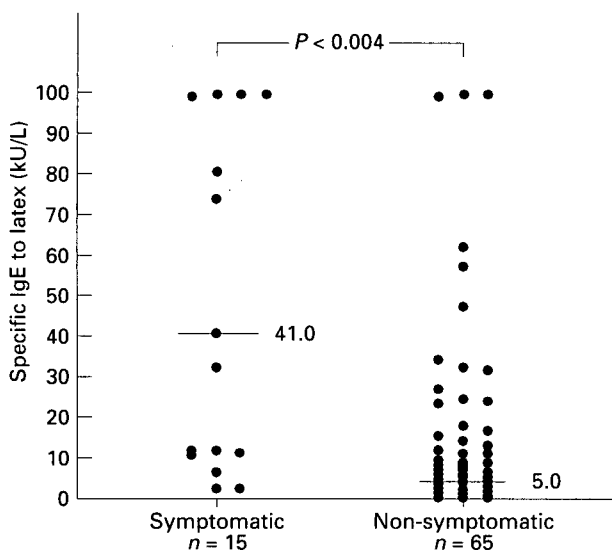


Fig. 2. Specific IgE to latex in symptomatic ($n = 15$) and non-symptomatic ($n = 65$) patients. Bars represent median values.

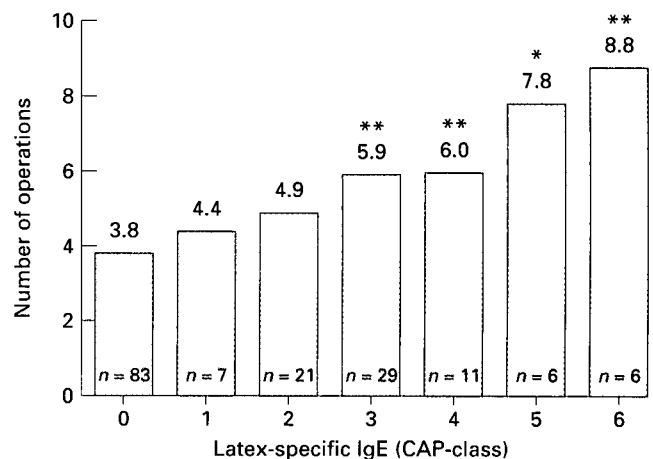


Fig. 3. Relation of concentration of specific IgE in serum to latex and numbers of operations. * $P < 0.03$, ** $P < 0.02$ (analysed by unpaired *t*-test) refer to children without latex-specific IgE.

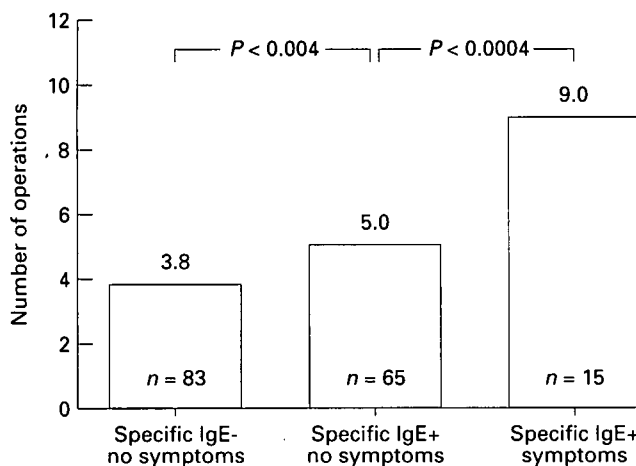


Fig. 4. Association of numbers of operations and state of sensitization or the occurrence of clinical symptoms.

sensitivity (data not shown). We therefore switched to SPT with natural latex milk.

The safety of skin-prick testing with latex has been the subject of controversy in the literature [13,14]. We did not observe appreciable side-effects of SPT, even in four of our five patients who otherwise display systemic reactions; however, one patient was not skin-tested because of most severe clinical reactions in his history.

Clinically relevant allergy to latex

Systemic clinical symptoms occurred in 5/165 patients (3%) with spina bifida. Much more frequently (14%), mild to moderate symptoms were reported while inflating a balloon. Similar to our data, other authors reported 9.7% [15] and 12% [16] of spina bifida patients with symptomatic latex allergy.

Many patients, although sensitized to latex, did not report symptoms on contact with latex-containing material. This discrepancy is a well-known phenomenon in respiratory and nutritional allergy and is not completely understood. In patients with spina bifida, one could speculate that clinical symptoms may occur in the future in some of the sensitized patients. Long-term prospective follow-up studies on the time-course of sensitization and allergy in patients with spina bifida would be interesting for the characterization of early predictors.

Number of operations

We found a clear relationship between number of operations and degree of sensitization in our patients with spina bifida. According to our data, more than five

operations significantly increase the risk of sensitization to latex in patients with spina bifida. In accordance with our data, more than nine operations have been found in the literature to be a risk factor for anaphylactic reactions in children with spina bifida [17]. The average number of operations in the group of symptomatic patients was also nine. Surprisingly, our patient with the greatest number of operations (26 operations), a 27-year-old atopic man, was not sensitized to latex.

Atopic disposition

We found that 34% of latex-sensitized patients with spina bifida were atopic in terms of presence of specific IgE in serum to common environmental allergens. In the literature, figures from 27% [2] up to 83% [9] have been reported. However, the numbers of patients were small in these studies. In one study of risk factors, atopy and exposure were assessed as synergistic parameters [18]. In summary, atopy in the group of patients with spina bifida is represented much more frequently than in the general population, where latex allergy is believed to be less than 1% [19].

Control group

In the 144 sera from atopic children sent to our allergy laboratory, 17% were sensitized to latex. In a study from the USA, 24/200 sera (12%) from their allergy laboratory were positive for latex-specific IgE [20]. These data support a recent report on atopic children with symptomatic latex allergy focusing on the need for determination of specific IgE to latex even in children with no known risk factor for latex allergy, such as in severe atopic dermatitis [21].

Based on our data we conclude that in order to minimize risk of severe systemic clinical reactions, all patients with spina bifida should be screened for their individual risk of latex allergy to allow preventive measures before operations. Risk factors for latex allergy seem to be more than five operations, atopic predisposition, history of clinical symptoms while inflating a balloon, and a sensitization with a CAP-class of ≥ 4 . More studies, especially with provocation tests, are warranted to further specify predictors for severe anaphylactic reactions.

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