

Outcome of a latex avoidance program in a high-risk population for latex allergy – a five-year follow-up study

N. Reider, B. Kretz, G. Menardi*, H. Ulmer† and P. Fritsch

Department of Dermatology and Venereology, *Department of General Surgery, Working Group of Pediatric Surgery, and †Department of Biostatistics and Documentation, University of Innsbruck, Austria

Summary

Background Children with a shunted hydrocephalus are at highest risk for developing an immediate type allergy to latex. Limited data are available for preventive or therapeutical approaches.

Objective To evaluate the effectiveness of latex avoidance, with special regard to status of sensitization and compliance.

Methods In 1995, 131 children with a shunted hydrocephalus were screened for sensitization to latex by skin prick test and determination of specific IgE. Patients and parents were instructed on latex-avoiding strategies. Hospital physicians, family doctors and dentists were advised to perform further surgical and other medical interventions under latex-free conditions.

In 2000, 100 of these 131 patients were re-evaluated according to the same testing procedures. Special attention was directed at the extent prophylaxis had been performed.

Results In 1995, 30/100 patients re-evaluable in 2000 proved sensitized to latex, 70 had negative testing results. In 2000, 64/70 patients were still negative, six had meanwhile developed latex-specific IgE. Seven out of thirty subjects with former positive testing had changes within the same RAST-class, 20 showed a decline of at least one RAST-class, whereas in three cases an increase of latex-specific IgE was found. However, only 34 patients, mainly those being already sensitized, had thoroughly followed both medical and private prophylaxis. Within this group, 16 subjects (47.1%) had improved and another nine (26.5%) were still negative. Only three (8.8%) already previously sensitized patients presented with a further increase of latex-specific IgE. Medical prevention contributed more to the outcome than home prevention. No statistically significant correlation with latex-avoidance was observed, however, in previously unsensitized subjects. Underlying disease, atopy, number of operations, and age did not prove as significant variables.

Conclusion Secondary prevention results in a decrease of specific IgE in latex-sensitized patients with hydrocephalus. This is due to medical more than home prophylaxis. Sensitization obviously occurs mainly in early childhood, thus primary prevention remains to be the main target.

Keywords latex allergy, spina bifida, prevention

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Introduction

Around 70 years ago, the first case report on anaphylaxis due to contact with natural rubber was published, but only in the past two decades has latex been recognized as an important aetiological agent of IgE-mediated allergic reactions. The National Centre for Biotechnology Information (PubMed) lists 1000 papers published since 1994 alone. Numerous studies identified health care workers, workers in the rubber industry, and individuals with histories of atopy, self catheterization and multiple

surgical procedures as risk groups [1–11]. The highest prevalence rates for latex-sensitization (29–55%) were reported for children with spina bifida or hydrocephalus of other causes [2, 3, 9]. Eliciting allergens and their molecular structures [12–18], and cross-reactions to flowers and foods [19–23] have been investigated thoroughly (for review see [24]). Several recommendations for primary, secondary and tertiary preventive measures have been published [25–29] but only limited data are available on their effectiveness [30–35]. This prompted us to perform a prospective study on the outcome of a latex avoidance program in a cohort of 100 children with shunted hydrocephalus over a comparatively long observation time of 5 years. Special attention was given to the dependence of our results on the status of sensitization prior to the study, compliance, and potential confounding factors.

Correspondence: Dr Norbert Reider, University of Innsbruck, Department of Dermatology and Venereology, Anichstrasse 35, A-6020 Innsbruck, Austria. E-mail: norbert.reider@uibk.ac.at

Patients and methods

From March 1995 to February 1996, 131 children with shunted hydrocephalus, either associated with spina bifida (48) or of other origin (83), referred to our Department by the Division of Pediatric Surgery, were screened for sensitization to latex by skin prick tests, specific IgE assays and, occasionally, by a latex glove exposure test, as described below. Forty-one out of one hundred and thirty-one children (31%) were found sensitized [36] and provided with a medic alert card. This contained the message 'Type I allergy to latex – risk of fatal shock – avoid use of latex (gloves, mucosal contact, surgery)' as most important catchwords. All patients (both sensitized to latex and not) and/or their parents, respectively, were then informed on the hazards of latex allergy and instructed on preventive measures orally and by a written handout. Instructions comprised information on origin and manufacture of natural rubber latex, but also on rubber components which induce contact dermatitis only, like vulcanizers or accelerators. We further compiled a list of latex-containing products frequently used in daily life, and latex-free alternatives. As far as possible, we tried to provide trade names or at least terms for non-latex rubber (like 'silicon', 'vinyl', 'lycra'). Risk factors, routes of sensitization, and signs and symptoms of latex allergy from contact urticaria to anaphylactic shock were explained, emphasizing the most hazardous forms of exposure like anaesthesia, latex gloves, condoms, catheterization, inhalation and other forms of mucosal contact. Patients were also provided with an emergency kit, containing an oral antihistamine, a soluble corticosteroid, an inhalative epinephrine spray, and an epinephrine autoinjector. Issues of 'home prophylaxis (HP)' – avoidance of contact with balloons air-mattresses, clothes, condoms, toys, pacifiers, gloves, and flowers or foods known to cross-react with latex allergens, etc. – as well as of 'medical prophylaxis (MP)' – avoidance of latex gloves for physical examinations, hygienic body care, surgical and dental procedures, and of latex catheters, masks, etc. were explained comprehensively. Moreover, we informed patients on self-help associations and web-sites relevant to the subject, and advised them to also forward all information to kindergarten and school teachers. In an attempt to grant a latex-free environment for all further surgical and other medical interventions, a letter of information was circulated to all surgeons, anaesthesiologists, family doctors and dentists involved in the care of the patients. At our surgical departments, the following regulations were introduced: information was obtained from the manufacturers on possible latex components within the complete equipment used for anaesthesia, and latex-free alternatives were provided. Concerning operations, we recommended the following procedure to the anaesthesiologists: Operations in high-risk patients (sensitized or not) should principally be performed in the morning, and latex-containing devices removed from the operating theatre the preceding evening. No staff (including those who did not deal directly with the patient) should be allowed to carry latex gloves during surgery.

Periodical annual controls at the allergy unit were suggested to the paediatricians.

One hundred of this original series of 131 subjects were available for a follow-up evaluation from April to August 2000. Of these, 47 patients were females, 53 males, with a mean age of 11.61 years (range 1–27) in 1995. Forty-four were

suffering from spina bifida, 56 from other causes of hydrocephalus. In the 1995 investigation, 30/100 patients had proven sensitized against latex, 70 had had negative test results, eight had had a history of anaphylactic reactions related to contact with latex, ranging from contact urticaria (exposure to air-mattresses, balloons, catheters and other medical devices), dyspnoea (inhalation of latex particles from balloons and powdered gloves), to anaphylactic shock during surgical interventions. Daily catheterization had been performed by 31 patients with spina bifida and by seven with other types of hydrocephalus. Latex catheters had been used until 1994/95 and were then replaced by silicon ones. The mean number of previous surgical interventions per patient before 1995 had been 8.31 (range 0–35).

The test procedures performed in 1995 and 2000 were as follows: For skin prick tests, an ammoniated natural latex milk, mean protein content 42 µg/mL (Regent Hospitalprodukte, Mönchengladbach, Germany) was used. Skin prick tests were carried out on the volar surface of the forearm, with normal saline and histamine hydrochloride (10 mg/mL, ALK) serving as negative and positive controls, respectively. Results were read after 15 min. Weals at least half the diameter of histamine and 3 mm or larger were regarded positive, according to EAACI guidelines [37].

Latex-specific IgE were determined by the standard RAST technique (AutoCAP® system, Pharmacia, Uppsala, Sweden). IgE levels ≥ 0.35 kU/L (class 1) were considered positive.

Sensitization to latex was defined as evidence of both positive RAST and skin prick tests. As shown previously [3, 38], this allows for sufficient sensitivity and specificity. As opposed to 'sensitization', latex 'allergy' was defined as sensitization plus a history of allergic reactions upon contact with latex. In inconsistent cases, patients were challenged according to [39] by applying a piece of latex glove (Sempermed, Semperit, Vienna, Austria) for 15 min on a wetted finger, a piece of vinyl glove on another as a control. Itching, weals and flares were considered positive reactions. When negative, a whole glove was applied to the wetted hand for another 15 min. For ethical reasons (compare also [24]), challenge tests were not performed in all patients, as most of them were severely physically and mentally disabled.

All patients were carefully interviewed employing a specifically designed questionnaire in order to assess the amount of latex exposure since instructions on latex avoidance had been given in 1995. Specific points raised were precautions performed to avoid latex, type of urinary catheters, contact with other latex-containing medical devices and domestic products, number, circumstances and symptoms of anaphylactic reactions related to latex, or food and flowers known to cross-react with latex. Furthermore, number and kind of past surgical/dental operations, and if these were performed under latex-free conditions, intercurrent diseases and premedication, atopy and concomitant allergies, were recorded from the patients and their physicians.

Patients who were classified as (-MP) or (-HP) had not bothered about latex exposure in any way.

As a measure for the efficacy of secondary prevention, besides history, changes in latex-specific IgE of at least one RAST-class between 1995 and 2000, were considered relevant. Although skin prick tests had proved a valuable tool for the diagnosis of sensitization to latex, we did not include differences of

weal sizes between 1995 and 2000 into our evaluation, as it is known that this is age-dependent in children [40] and, moreover, reflects changes in the degree of sensitization only to a limited extent [41].

Statistics

Changes of latex-specific IgE in correlation to the extent of latex-avoidance was analysed using contingency tables and two-sided Fisher's exact test. *P*-values <0.05 were considered statistically significant.

Results

Rast

Sixty-four out of the 70 patients who had not shown latex-specific IgE in 1995, were still negative in 2000, the remaining six had become positive (Table 1). Of the 30 patients with positive RASTs 1995, nine had become negative and 11 others had RASTs at least one class lower (mean decrease of the 20 'improved' patients 1.43 classes). Seven were still positive within the same RAST class ('unchanged'), and only three children had (at least one class) higher RAST values (mean change 1.67 classes). In absolute kU/L-counts, the mean decrease was 8.97 kU/L (range 0.49–59.8) from an average starting value of 12.28 kU/L, the mean increase was 2.51 kU/L (range 0.38–7.47). Within the subgroup of the 'unchanged', four patients experienced a mean increase of specific IgE of 1.55 kU/L, three a decrease of 1.98 kU/L.

Skin prick tests

Eight of 9 subjects who had become negative in RAST, also showed a negative skin prick test in 2000, compared to only two of 11 with at least one-class decreased but still positive results.

History

The mean number of surgical treatments between 1995 and 2000 was 1.76 (range 1–10). No allergic complications had occurred during any of these interventions, but nine patients had experienced latex-associated anaphylactic reactions in situations not related to medical procedures, four of them for the first time. Among the latter, two showed an increase, and two a decrease of specific IgE. Among the five subjects with a history

of latex-related anaphylaxis before and after 1995, two showed the same RAST-class, two a decrease, and one an increase. No reactions had occurred in patients whose specific IgE had fallen below the detection limit. The analysis of the questionnaires revealed that latex avoidance according to the recommendations given in 1995 had been executed in only a minority of patients: as few as 34/100, mainly those who had proven sensitized already in 1995, had been subject to both MP and HP. HP was practised by 70/100, and MP in 36/100 subjects or their physicians, respectively. Twenty-eight patients had not employed any preventive measures at all. The low compliance of the physicians was particularly surprising: With few exceptions, only the already sensitized patients had been operated in a latex-free environment, and only a small minority of the patients had been referred for periodical reevaluation of their status of sensitization during the observation period.

Impact of avoidance strategies on latex sensitization

Patients practising both MP and HP (n = 34) Nine subjects were still negative at follow-up, in 16 latex-specific IgE had decreased for at least one RAST-class. Six patients had remained stably positive, but three had developed further increases. Together, significantly more patients showed decreased or persistently negative IgE than increases (*P* < 0.001).

Patients subject to neither MP nor HP (n = 28) Twenty-six subjects had negative IgE in both 1995 and 2000, one remained stably positive, one was newly sensitized.

Patients practising HP alone (n = 36) Twenty-eight patients remained negative, three had decreased IgE values (8.3%), but five (13.9%) proved to be newly sensitized.

Patients subject to MP alone (n = 2) One remained negative, and one had decreased IgE.

Conversely, within the total of 20 patients with decreases of their specific IgE, 16 (80.0%) had followed both MP and HP, one (5.0%) MP alone, and three (15.0%) HP alone. Among the nine children with increases of their IgE, however, only three had followed both MP and HP, five HP only, and one neither MP nor HP.

Influence of underlying disease, atopy, number of operations, and age on the outcome of latex prevention

Significantly more patients with spina bifida (56.3%) than with other causes of hydrocephalus (16.9%) had proven sensitized against natural rubber latex in 1995. Relatively more spina bifida patients were available for follow-up in 2000. However, changes of specific IgE during the observation period were equally distributed between both groups.

Sensitization against latex had been observed more frequently in atopic patients (43.9%) than in non-atopic (15.5%) in 1995. The corresponding numbers at follow-up were 51.9% and 17.8%, being not significantly different to the proportion before.

The mean number of operations within the observation period and age at inclusion were of no significant influence on both the extent of latex prevention efforts and changes in specific IgE levels (data not shown).

Table 1. Changes of RAST-classes from 1995 to 2000

		2000				
		Class 0	Class 1	Class 2	Class 3	Class 4
1995	Class 0	64	2	3	1	
	Class 1	4	1	1	1	
	Class 2	4	2	4	1	
	Class 3	1	1	4	2	
	Class 4			1	2	
	Class 6					1

Numbers in bold show patients without change, lower-left half shows patients with a decrease of specific IgE, upper-right half shows those with an increase of at least one RAST-class. *n* = number of patients. RAST-classes: 0–0.35 kU/L = class 0, 0.36–0.70 = class 1, 0.71–3.5 = class 2, 3.6–17.5 = class 3, 17.6–50 = class 4, 50.1– = class 5, >100 = class 6.

Discussion

There are several recommendations for the preventional and therapeutical approach to populations being at high risk for latex allergy or subjects already sensitized, that have been issued during the past few years [25–28], but only limited data are available concerning the outcome of these efforts. In a recent report [42], 88% of 16 anaesthesiologists with initially positive RASTs experienced a decrease in latex-specific IgE 10–15 months after the hospital had replaced all latex examination gloves with vinyl and nitrile gloves. Similar encouraging results were observed in health care workers by another group [33]. Cremer et al. [34] performed a follow-up in 67 children with spina bifida. The authors attributed the favourable outcome of this study mainly to latex-free conditions in the operating theatre. In another publication [35], the authors demonstrated a time-dependent (though not significant) decrease in mean latex-specific IgE of patients with spina bifida, after surgical interventions had been changed to be performed latex free.

On the other hand, a recent study by Ylitalo's group [32] shows the practical difficulties for patients to translate latex avoidance into action: although carefully and comprehensively advised, a great majority of their cohort reported further latex contacts at follow-up. Also, no decrease in skin prick test reactivity, latex RAST or IgE levels to major latex allergens developed over a period of 2.8 years. Mazon et al. [30] even observed a 5:1 ratio of increases over decreases in a two years follow-up of children with spina bifida who were also advised on HP and MP.

Our own study presents the outcome of secondary preventional strategies in the hitherto largest cohort of subjects at high risk for latex allergy for a comparatively long follow-up period. In addition, it considers the outcome of these efforts in dependence on the actual extent of latex avoidance and the development in primarily unsensitized subjects, two aspects of substantial practical relevance which have hardly been taken notice of in the literature. Several conclusions may be drawn from our data:

- Secondary prevention appears to be effective in already latex-sensitized persons. This is in good agreement with previous studies discussed above [33, 42]. Among our patients who had followed both MP and HP, 64.0% of those who were positive 1995 showed at least one RAST-class decrease in latex-specific IgE (below the limits of detection in seven cases), and no new case of sensitization had developed.
- Latex appears to induce specific IgE in children predominantly during early childhood, whereas the risk of sensitization obviously declines at later ages, as the majority of non-compliant patients had not been sensitized in 1995 and, surprisingly, remained so in 2000. It was found earlier that latex allergy develops less frequently in adult patients with spinal cord injury and multiple surgical interventions [43]. The same conclusions were drawn from a recent study [44] in which adult patients with spinal cord injury were compared to children with spina bifida and similar rates of operations and atopy. We have to be aware, however, that in our study relatively more patients with spina bifida than with hydrocephalus of other origin were available for follow-up. This may lead to a potential bias, as children with spina

bifida usually undergo surgical interventions already during the first days of their lives. However, no differences in the change of specific IgE between both groups could be observed.

- The main objective in the management of latex allergy must therefore still be primary prevention. This is also corroborated by a study [31] in which no case of sensitization was observed in a series of 12 high-risk newborns during a 2-year follow-up period following the introduction of latex-free surgical conditions, compared to 3/7 children in a comparable period before.
- Medical prevention is more relevant than home prevention. Both Ylitalo's [32] and our trial show that it is unrealistic to expect systematic avoidance of latex in everyday life, especially in patients whose test results are negative and thus do not feel threatened, and due to the impossibility to detect all sources of latex. Moreover, our data indicate that HP, compared to MP, does not contribute significantly to the outcome of latex avoidance strategies. This is in good correspondence with other groups [31, 35] who also concluded for spina bifida patients that 'surgery without strict latex prophylaxis is the main cause of new sensitization and worsening of preexisting latex antibody levels' [34]. Thirdly, antigens involved in latex allergy are not the same in different risk groups [11, 12, 14, 15], and sensitization in spina bifida mainly occurs by mucosal contact rather than by inhalation. The low degree of compliance among the physicians involved in the care of the patients outside our hospital was particularly surprising and disappointing. Our attention must thus be directed to even enhanced educational campaigns among health care workers of all fields. As a matter of course, latex-sensitized patients should nevertheless be advised to avoid every extensive latex contact in daily life, like balloons, mattresses, condoms or gloves.

Finally, it must be stressed that secondary prevention, as performed in our study, resulted in significant changes at least of the laboratory findings. This, however, is not tantamount to loss of clinical reactivity, as 3/20 patients with decreasing IgE experienced latex-related incidents again. Loss of sensitization may have occurred in those nine subjects whose latex-specific IgE fell below detectable limits, and who had not experienced anaphylactic events any more. In nearly all these cases, the prospective clinical value of negative RASTs was further supported by negative skin prick tests, in contrast with the children with decreased but still positive RASTs, who in most cases remained positive in prick tests.

In conclusion, our data suggest that secondary prevention in latex-sensitized patients results in a significant decrease of latex-specific IgE, at least in children with spina bifida and other causes of hydrocephalus. Within this risk group, MP appears to be more relevant than HP, and sensitization obviously mainly occurs in early childhood. Thus, primary prevention remains to be the main objective. Threshold allergen exposure levels for sensitization and eliciting allergic reactions are not defined [45]. They may depend on the route of exposure and sensitization and may thus vary between different risk groups like health care workers and atopics. Prevention programs must thus be established on an individual basis. Specific immunotherapy may be a promising tool for future therapy of latex allergy.

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