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Latex sensitisation and allergy in children with myelomeningocele

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Abstract *Introduction:* Children with spina bifida (SB) have a high degree of exposure to latex products as a consequence of repeated surgical procedures, implantation of latex-containing materials and catheterisation. The consequence is a higher incidence of latex allergic reactions. *Objective:* The aim of this study is to evaluate the prevalence of latex sensitisation and allergy in a population of children with myelomeningocele (MMC) and to assess the role of associated risk factors. *Results:* Forty-eight percent of the patients (29

out of 60) showed a latex sensitisation with specific IgE >0.7 kU/l while 15% (9 out of 60) were allergic to latex (specific IgE >0.7 kU/l and clinical manifestations). The principal factor correlated with allergy to latex was specific serum IgE to latex (radioallergosorbent test [RAST]) values ($p < 0.01$). Other factors were total serum IgE (paper radioimmunosorbent test [PRIST]) values, number of surgical procedures and familiarity with allergy. *Conclusion:* These results underline the importance of prophylactic measures to avoid the exposure, not only in the sanitary environment, through the institution of latex-safe routes, but also in daily life, to prevent potentially serious allergic reactions.

Keywords Latex allergy · Myelomeningocele · PRIST · RAST · Surgical procedures · Sensitisation

Introduction

Children with myelomeningocele (MMC) have a high degree of exposure to latex products through repeated surgical procedures, catheterisation and implant of latex-containing material. This has led to a higher incidence of IgE-mediated allergic reaction in this group of patients, who are at risk of several severe and unexpected allergic reactions related to surgical procedures [1].

Allergy to latex is a clinical manifestation of type 1 (immunoglobulin IgE-mediated) hypersensitivity to latex. Clinical manifestations involve urticaria, angioedema, rhinitis, conjunctivitis, asthma and generalised anaphylactic

reaction [2]. Serious systemic reactions usually occur after mucosal exposure to latex devices or during surgical procedures, but may also occur under a variety of other circumstances in daily-life. Although there is a distinction between latex allergy with clinical reactions and latex sensitisation in which the presence of latex specific IgE antibodies has caused no clinical symptoms, children with MMC who are sensitised to latex are at higher risk of clinical reactions, including anaphylactic reaction during meningeal exposure to latex devices.

As reported in the literature, the prevalence of sensitisation to latex among children with spina bifida (SB) may be as high as 64% [3], and it is considered the highest

prevalence in the general population [4, 5]. Other risk groups like health care workers and other multioperated patients are not at the same risk [4–6]. The causes and risk factors to latex allergy associated with SB are not still well understood [3–6].

The aim of the present study was to evaluate the prevalence of latex sensitisation and allergy in a population of children with myelomeningocele followed in the Spina Bifida Centre of the Policlinico Gemelli, Rome, and to assess the role of associated risk factors, e.g. atopy and number of surgical procedures.

Materials and methods

Sixty young patients (26 boys and 34 girls) with myelomeningocele aged between 1 and 22 years (mean age 7.6 years) admitted for routine periodic controls to the Spina Bifida Centre of the Catholic University of Rome were enrolled in the present study; of these, 51 had a ventricular–peritoneal shunt for hydrocephalus. Each patient and parent was informed about the study, and they gave their consent to participate.

We acquired personal data by asking each patient or parent to complete a case form. Questions specifically concerned the following issues: possible risk factors for sensitisation, like the presence of other allergic reactions in the patients (rhinitis, asthma, dermatitis) or in their close blood relations (parents, brothers, grandparents), the presence of adverse reactions to foods or allergic reactions occurring in the pre–post surgical period or during other types of exposure to latex, the number of surgical interventions and particularly the presence of adverse reactions after the use of latex devices (gloves, balloons, dummies).

During the follow-up programme, 5-cm³ venous blood samples for total IgE (paper radioimmunosorbent test [PRIST]), specific IgE to latex (radioallergosorbent test [RAST]) and eosinophil cationic protein (ECP) was obtained.

Specific IgE to latex were measured using an immunoenzymatic method (UniCAP System; Pharmacia, Uppsala, Sweden) and the manufacturer provided the reference values. Results were classified as class 0 for values lower than 0.35 kU/l, class 1 for values between 0.35 and 0.7 kU/l, class 2 for values between 0.7 and 3.5 kU/l, class 3 for values between 3.5 and 17.5 kU/l, class 4 for values between 17.5 and 50 kU/l, class 5 for values between 50 and 100 kU/l and class 6 for values greater than 100 kU/l. Values greater than 0.70 kU/l were considered positive. Latex sensitisation was defined as the presence of a positive RAST result for latex. Latex allergy was defined as the presence of clinical manifestations to latex in sensitised patients. Patients with a positive history of allergic reactions to other allergens (implants, foods) were considered atopic.

In the final analysis, the prevalence of sensitisation and allergy to latex was calculated. The relationship between latex sensitisation and atopy, number of surgical procedures,

personal and family history of allergic reaction and sensitisation to food allergens was determined.

Sensitivity, specificity, positive and negative predictive values and accuracy of tests for diagnosis of latex allergy and sensitisation were calculated using standard definitions.

The statistical analysis was carried out using the STAT-SOFT96. Comparison between sensitised vs. non-sensitised patients and allergic vs. only sensitised patients was assessed using the one-sample *t* test. Statistical significance was considered to be $p < 0.01$.

Observations and results

On the basis of the anamnesis we found that all patients with MMC included in our study, had undergone between 1 and 16 surgical procedures (mean 4.3) and all had undergone at least one procedure.

Thirty patients (50%) had a positive history of other allergic reactions and we considered them atopic; 31 patients (52%) had at least one allergic family member (parents, sisters or brothers, grandparents).

All 60 patients had values of total serum IgE between <200 and 6,000 kU/l (mean value 370.4 kU/l), while the RAST values ranged from <0.35 to 110 kU/l (mean value 8.69 kU/l; Table 1).

Table 1 Comparison between sensitised vs. non-sensitised patients. *DVP* ventricular–peritoneal shunt, *PRIST* paper radioimmunosorbent test, *RAST* radioallergosorbent test, *ECP* eosinophil cationic protein

	Total	Sensitised	Standard deviation	Non-sensitised	Standard deviation
Patients	60	29		31	
Gender (male)	26	15		11	
Surgical procedures (mean)	4.3	5.8		3	
DVP	51	29		22	
Atopic	30	20		10	
Familiarity	31	20		11	
PRIST mean (kU/l)	291	533*	1,457	74	153.2
RAST mean (kU/l)	8.69	18.4**	25.8	<0.35	0.06
ECP mean (µg/l)	36.5	38	31.1	34.9	44.1
Age (mean years)	7.6	10		5.6	

* $p < 0.01$

** $p < 0.01$

Among the patients, 29 (48%) had RAST >0.70 kU/l for latex and they were considered sensitised. In the sensitised group, all patients (29 out of 29) had the ventricular-peritoneal shunt, while only 22 out of 31 (70%) had it in the non-sensitised group (Table 1).

Nine patients (15%) had shown clinical manifestations during exposure to latex (all had urticaria–angioedema syndrome, 2 associated with oculorhinitis, 3 with respiratory symptoms), while 3 of them were during surgical procedures. These nine patients were considered allergic to latex (RAST positive and clinical symptoms). The other 20 of the sensitised patients had specific IgE levels >0.7 kU/l, in spite of the fact that they were asymptomatic.

Patients with latex sensitivity had undergone more operations than non-latex-sensitised patients (mean value 5.8 vs. 3 surgical procedures). Sensitised patients were about 10 years old vs. 5.5 years in the group of non-latex sensitised patients (Table 1). All sensitised children were operated on during the first year of life.

The mean value of the specific IgE to latex in the sensitised group was 18.4 kU/l (range 0.7–110 kU/l). Concerning RAST class, we have observed that 11 patients belonged to the RAST class 2, 10 to class 3, 6 to class 4, 1 to class 5 and 1 to class 6. A difference between the values of the specific serum IgE of the symptomatic group (9 patients) and those of the sensitised non-symptomatic one (20 patients) was observed: respective mean values were 36.6 kU/l (range 1.29–110 kU/l) and 11 kU/l (range 0.88–41 kU/l; $p<0.01$; Table 2).

Comparing symptomatic patients with only sensitised patients we have seen that 6 out of 9 (66%) patients in the first group were in RAST classes 4–6, while only 2 out of 22 (9%) patients in the second group were in RAST class 4.

Paper radioimmunosorbent test values were associated with sensitisation. The sensitised patients showed mean values of 533 vs. 74 kU/l of the non-sensitised patients ($p<0.01$). On the contrary, no statistically significant correlation was observed between PRIST values of allergic patients with respect to the sensitised group.

The presence of other allergies in the family and/or atopy turned out to be significant for sensitisation: 66% of the sensitised patients had at least one allergic family member, vs. 33% of the non-sensitised patients; similarly, in the sensitised group we observed 66% of patients with atopy, but only 33% of patients in the non-sensitised group.

The ECP values ranged between 2.39 and 210 $\mu\text{g/l}$, without a statistically significant correlation with the sensitisation to latex between the sensitised and non-sensitised groups (mean values 38 vs. 34.9 $\mu\text{g/l}$).

No differences regarding the sensitisation or the development of clinical allergy were observed between the sexes.

Also, although without statistical significance, we have found differences between the symptomatic and the non-symptomatic children regarding risk factors such as the number of surgical procedures, atopy and familiarity. In fact, children with clinical allergy to latex were subjected to more surgical procedures (mean value 6.5 vs. 4) and consequently they were older than the others (mean age 9.5 vs. 7.4 years).

Discussion and conclusions

Spina bifida is a pathology burdened with the necessity of numerous surgical procedures.

As reported by Bohle et al. [7] the prevalence of sensitisation to latex among children with SB may be 29–72%, and it is considered the highest prevalence in the general population [5–7]. Other risk groups like health care workers and other multioperated patients are not at the same risk. The causes and risk factors of latex allergy associated with SB are not still not well understood.

In the present study about 50% of the patients showed a sensitisation to latex (specific IgE >0.7 kU/l), and the increased number of surgical interventions was associated with a higher risk of becoming sensitised, but only 15% of patients had a clinical allergy. These results agree with those reported by Cremer et al., Szepefalusi et al. and Buck et al. with a prevalence of sensitisation of 55, 56 and

Table 2 Comparison between symptomatic vs. non-symptomatic patients

	Sensitised	Symptomatic	Standard deviation	Non-symptomatic	Standard deviation
Patients	29	9		20	
Gender (male)	15	5		9	
Surgical procedures	5.8	6.5		4	
DVP	29	9		20	
Atopic	20	8		12	
Familiarity	20	8		12	
PRIST mean (kU/l)	533	670	1,120	469	854
RAST mean (kU/l)	18.4	36.6*	14.5	11.13	18.9
ECP mean ($\mu\text{g/l}$)	38	43	32.5	36	30.1
Age (mean years)	10	9.5		7.4	

* $p<0.01$

47.6% respectively [8–10]. Although the sensitisation, i.e. the positive of the specific IgE and/or the skin tests, is not equivalent to a clinically expressed allergy, these patients are considered to be at high risk of anaphylactic reactions when contact with products containing latex occurs. As reported by Moneret-Vautrin et al., the anaphylactic reaction is more frequent in children with SB compared with the general population [11]. In fact, as Buck et al. affirmed [10], shunt systems are latex free and exposure is probably due to glove powder left on the meninges. There is not a specific correlation between latex sensitisation and the number of intra-abdominal procedures [12], which emphasises that meningeal contact may be a predisposing factor in these children [10]. It has been hypothesised that since rubber particles are water insoluble, they do not transfer from glove to skin in health care workers, but could be transferred to the body cavity mucosal membranes of MMC patients by the meninges during repeated and closer neurosurgical operations [5].

In children with MMC compared with other forms of SB or hydrocephalus alone who are exposed to a lower risk of sensitisation to latex [9], early exposure to an allergen like latex might consolidate the neonatal response, precluding the normal th2–th1 switch and inducing future allergic responses [13]. Furthermore, it has been demonstrated that being born during pollen season increases the risk of pollinosis [14].

All the sensitised patients had the ventricular–peritoneal shunt, confirming literature reports that underline that patients with ventricular–peritoneal shunts are at higher risk, probably because they undergo a significantly higher number of neurosurgical operations than patients without it, but on the contrary, the ventricular shunt per se does not seem to be an independent risk factor [10].

With regard to other risk factors, in our population, sex and age are not particularly determining factors. In fact there is no significant difference between females and males concerning sensitisation or the appearance of clinical allergy to latex. The incidence of sensitisation is higher with increasing age and the cause may be found in the increased number of surgical procedures.

Among the risk factors for latex sensitisation, the repeated exposure to latex devices during repeated operations has been well demonstrated in the literature. The number of surgical interventions is directly correlated with sensitisation and the allergy, like the values of the specific IgE to latex [3, 8, 15]. On the other hand, some authors reported that the number of surgical interventions could be related to other risk factors, as reported by Szepefalusi, which underlined that the percentage of sensitisation to latex in children with MMC is really higher than that observed in adults with injuries to the spinal column and multiple interventions.

This tendency to produce IgE latex protein binding is explained by a disorder mainly related to the pathology of SB itself and only secondarily to other factors, such as the number of exposures to latex and atopy [9].

We think that the sensitisation to latex may be related to two main events that must converge at the same time in the MMC patient. The first is predisposing conditions that are still unclear, like the early exposure to latex in MMC and the different latex proteins recognised in patients with SB [6]. The second is repeated exposure to latex by an effective method like meningeal exposure. According with Obojski et al.'s [15] studies in the two groups examined, the sensitised and non-sensitised patients, atopy represents a significant strong risk factor for sensitisation and for the appearance of symptoms [16]. It was present in 66% of our sensitised patients and in 90% of the symptomatic ones.

In our study, the mean RAST CAP value for latex was significantly higher among symptomatic than among asymptomatic patients, confirming the data of Bernardini et al. [16] and Mazon et al. [17], who found that high mean RAST CAP values for latex were a significant risk factor for symptoms of allergy to latex.

The nine patients who became symptomatic had correlation with atopy and the number of operations as major risk factors of risk for allergy [3, 18]. In fact, in our study the number of operations and atopy also correlated with the development of symptoms because they increased the RAST CAP values.

In order to identification the patients at risk, we think carrying out an accurate allergological test as screening, a careful evaluation of any clinical evidence of latex allergy in all SB patients before each operation, and a cart of latex products among the sanitary staff are fundamental requirements [19]. The specific IgE dosage by immunoenzymatic methods (RAST) has shown a sufficient sensitivity and specificity in order to evaluate the clinical reactivity of the latex-sensitised children with SB when the symptoms are not well known [20].

We think that the ideal solution for children with SB may be latex-free operating rooms, i.e. sterilised as regards the allergenic proteins of latex and used exclusively for the operations on these children from birth [8]. In our Spina Bifida Centre, this has already been carried out due to the close collaboration between neurosurgeons, nurses in the departments and the operating rooms, and with anaesthetists.

It is important to underline that, as has been shown in our study, not all patients became symptomatic during surgical or diagnostic procedures. This fact points out the importance of prophylactic measures to avoid exposure, not only in the sanitary environment, through the institution of latex-safe routines, but also in daily life, to prevent potentially serious allergic reactions.

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