

Short Report

Frequent IgE sensitization to latex, cow's milk, and egg in children with short bowel syndrome

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Children with short bowel syndrome (SBS) undergo frequent operations, so they are at risk for sensitizing to latex. There have been isolated reports of sensitization to food in these children. In a cross-sectional study, we assessed sensitization to latex, cow's milk, and egg with skin prick tests (SPT) and serum-specific immunoglobulin E (IgE) in 14 children with SBS. Data were collected about the number of operations with latex devices, serum total IgE, and history of feeding with milk formula. Ten children were sensitized to latex (specific IgE median: 6.7 kU/l, range: 0.5–33). Compared with those non-sensitized, sensitized children had significantly ($p < 0.05$) higher levels of serum total IgE in z-units (mean rank 3.25 vs. 9.2, respectively), and more operations with latex devices (mean rank 3.75 vs. 9). Eight children were sensitized to cow's milk, one with only positive SPT, the other seven with serum-specific IgE (median: 3.5, range: 0.5–21.1 kU/l), and five to egg (specific IgE median: 0.68, range: 0.58–2.17 kU/l). Except for some isolated days with cow's milk formula, the children had been initially fed with a diet without intact cow's milk proteins. Sensitization to latex, cow's milk, and egg is very frequent in children with SBS. They should be treated in a latex-free environment since the very early stages of the disease, and should be routinely studied regarding food sensitization, as this might contribute as an added factor in the chronic diarrhea of these patients.

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Massive intestinal resections in newborns or infants because of congenital or acquired conditions give rise to the short bowel syndrome (SBS). Parenteral nutrition through central venous catheters has been life-saving, but to overcome complications and keep access for parenteral nutrition repeated surgical procedures are needed. Thus, these children are at risk for developing latex sensitization.

Adequate nutrition is the limiting factor for the proper growth and development of these children. Milk is the main food used in the early months or even years of life, so any problems

with tolerance to foods could become a damaging factor for the outcome of these patients, as described in isolated reports of children with SBS and allergy to milk or to egg (1), that is another foodstuff which is quite often consumed but is very allergenic.

The aim of our study was to systematically assess the latex sensitization in children with SBS, and the associated risk factors, to confirm if they are really at risk, and to assess the sensitization to foods, specifically to cow's milk and egg, to evaluate if there is an association beyond chance.

Methods

A cross-sectional study was done in a group of 14 consecutively selected children with SBS. They were diagnosed based on the commonly used criteria of dependence on parenteral nutrition for at least 90 days after surgical therapy for congenital or acquired intestinal diseases (2), and were being regularly visited in the Paediatric Nutrition Unit of our hospital, which is a tertiary reference center for pediatric surgery. Data were collected about sex, age, number of operations with latex devices, and early history of milk feeding.

Skin prick tests (SPT) were made on the anterior surface of the forearm with commercial extracts of latex, whole cow's milk, and egg white (ALK-Abello, Madrid Spain), together with control solutions of buffered saline and histamine clorhydrate (1/1000). The wheals were measured 15 min later; those with a diameter of at least 3 mm were considered positive. A blood sample was obtained, to measure serum total immunoglobulin E (IgE) and specific IgE to latex, whole cow's milk, and egg white with the RAST-CAP® system (Pharmacia, Uppsala Sweden), according to the manufacturer's instructions. Results ≥ 0.35 kU/l of specific IgE were considered positive. A child was considered sensitized to an allergen if SPTs or specific IgE gave positive responses. The study was approved by the Local Ethics Committee and informed consent was obtained from parents or guardians and from older patients.

Statistical study

The statistical study was performed with the spss 10.0 software program (SPSS Inc, Chicago, IL, USA). Categorical variables were compared with the Fisher's exact test and continuous variables with the Mann-Whitney *U*-test. To test for association between continuous variables, Spearman's correlation coefficient was calculated. Values of $p < 0.05$ were considered significant.

Results

We studied 14 children (six boys) with a median age of 2.23 yr. Ten children (71.4%) were sensitized to latex, eight (57.1%) to cow's milk, and five (35.7%) to egg, although this allergen was not assessed in two patients. The raw data of the patients are shown in Table 1. The serum-specific IgE in those with positive results ranged from 0.5 to 33 kU/l (median 6.7) for latex, from 0.5 to 21.1 kU/l (median 3.5) for milk, and from 0.58 to 2.17 kU/l (median 0.68) for egg. The child with meconium peritonitis was not sensitized, but the children with other diseases could be sensitized to any of the three allergens. Clinical reactions with latex had been identified in two of the latex-sensitized patients (generalized urticaria). The number of operations in which latex devices had been used was significantly higher in latex-sensitized children compared with those not sensitized (mean rank 9 vs. 3.75, Mann-Whitney *U*-test, $p = 0.031$), as well as the levels of serum total IgE in z-units (mean rank 9.2 vs.

Table 1. Data on primary disease, age, risk factors for sensitization and results of sensitization tests

Disease	Age (years)	Surgeries with latex devices (No.)	Total immunoglobulin E z-units	Skin prick test			Specific IgE kU/l		
				Latex	Milk*	Egg	Latex	Milk*	Egg
NCE	13.9	2	1.98	—	—	ND	Neg	Neg	Neg
Malf	7.3	4	2.62	—	+	+	3.9	1.9	2.13
Hirsch	6	13	1.78	+	+	ND	28.5	18.7	ND
NCE	3.3	8	3.76	+	+	+	9.6	0.5	0.58
Malf	3.3	6	1.13	—	—	—	0.67	Neg	ND
NCE	3.2	4	1.93	—	—	ND	0.78	Neg	Neg
Malf	2.4	8	2.55	+	+	—	10.9	3.5	Neg
Perfor	2	10	5.8	+	+	ND	33	9	Neg
NCE	1.9	7	2.98	—	+	—	0.66	0.52	0.68
NCE	1.6	4	2.61	—	—	ND	0.5	Neg	0.61
NCE	1.3	4	0.98	—	—	—	Neg	Neg	Neg
Malf	1	8	4.98	—	—	+	16	21.1	2.17
Malf	1	6	0.61	—	+	ND	ND	Neg	ND
Mec Per	0.9	3	−0.58	—	—	ND	Neg	Neg	Neg

NCE, necrotizing enterocolitis; Malf, intestinal congenital malformation;

Hirsch, Hirschsprung's disease; Perfor, intestinal perforation;

Mec Per, meconium peritonitis.

*Whole cow's milk Neg: <0.35 kU/l; ND, not determined.

Table 2. Type of milk feeding, according to sensitization to cow's milk: number of patients and duration in days of the feeding of each patient

	Before first operation		After first operation	
	No.	Duration	No.	Duration
Cow's milk sensitized, n = 8				
StF	2	1/1		
BF	—		3	12/120/150
EHF	1	34	5 + 3*	Indefinite
None	5			
Not sensitized, n = 6				
StF	2	9/1	1	4
BF	2	3/4		
EHF	—		5 + 1*	Indefinite
None	2			

StF, standard formula; BF, breast feeding; EHF, extensively hydrolyzed formula.

*Includes those initially fed EHF plus those who switched from StF and BF.

3.25, $p = 0.016$). In sensitized patients, there was a positive correlation between the number of operations with latex and the levels of latex-specific IgE ($r = 0.826$, $p = 0.003$).

Most of the sensitized patients had no personal or family history of atopy. This was present in only three of the children: they were sensitized to latex, milk, and two of them to egg, which was not tested in the third one. Two of them were also sensitized to other allergens (peach, walnut and peanut in one patient, soy and almond in the other). An additional patient, without family history, was sensitized to the three studied allergens and also to mites and *Alternaria*. All the children had received antibiotic treatment to prevent bacterial overgrowth.

Only two of the eight sensitized children to milk had been given standard milk formula before being operated, as shown in Table 2. After the first operation, all were breast-fed or given extensively hydrolyzed (EH) formula. When children grew older, although they were recommended to avoid cow's milk, transgressions happened and patients could be given uncontrolled foods containing variable amounts of milk. In two of these sensitized patients, evident immediate clinical reactions had been identified when given cow's milk; one had urticaria, the other rhinoconjunctivitis, associated with clear worsening of their stool pattern in both of them. The eleven children younger than 3.5 yr were being given elemental or EH formula; because of their deficient clinical and nutritional status, challenge with cow's milk for this study was not considered ethical and was not performed.

Discussion

Atopic children are at risk for latex sensitization and allergy (3, 4), but the highest prevalence is

found in those with spina bifida, although there are great differences between northern and southern countries (5, 6). Children with multiple surgeries for other diseases are also at risk (7). In our group of SBS children, we found a prevalence of 71.4%, and similar to other studies we found an association of latex sensitization with the number of operations with latex devices and with higher levels of serum total IgE (7). The high prevalence of sensitization in our patients is in contrast with the low prevalence found in spina bifida patients from South Africa (5). Differences in sensitization have been attributed, among other factors, to hygiene and Western life style, and in fact, children in the South Africa study came from a poor community of low socioeconomic status, while ours had been admitted to the hospital for long periods of time, and all of them had received several courses of antibiotic treatment.

Specific IgE to latex is quite a reliable index of clinical sensitivity, and it is known that about half of latex-sensitized patients present symptoms, but these were clearly identified only in two of our patients. However, as sensitization is a dynamic process and the first symptom can be a life-threatening reaction (7), latex-avoiding measures must be implemented in these children since the first operation.

Allergy to milk has sporadically been described, but not systematically assessed, in children with SBS (1). Prominent eosinophilia was found in colonic biopsies of nine infants with SBS and non-infectious bloody diarrhea, and attributed to food allergy, although without a study of specific foods (8). Rectal bleeding ceased if formula feeding, mainly EH formula, was decreased or withheld. There are reports which associate necrotizing enterocolitis (NEC) and intolerance (non-IgE mediated allergy) to cow's milk proteins (9, 10). This hypersensitivity was diagnosed after the onset and treatment of NEC, so there are no data regarding the chronologic order of the events. In other diseases, like congenital malformations, an etiology of cow's milk allergy does not seem plausible, so we must assume that sensitization takes place after the first operation. Ours was a cross-sectional study, so it cannot offer further information.

Regarding the source of allergens, standard milk formula was used before the first operation in just two of our sensitized patients, and only for 1 day each. Afterwards, all children were breast-fed or given EH or elemental diets, but still some got sensitized. Sensitization could begin when they were given solid foods containing milk proteins, but cow's milk proteins have been also

found in human milk (11), and the allergenicity and sensitizing role of residual epitopes in EH formulas cannot be ruled out (12). As for egg, we could not get reliable data about its consumption. Sensitization to egg in infants who have not started eating it is known since long ago (13), so antenatal or via the breast sensitization is thought to occur.

Food sensitization may cause digestive symptoms, including chronic diarrhea. This is also characteristic of SBS, because of an insufficient area of mucosal intestinal surface. If there is no clinical manifestation in other organs, the effect of a food allergy on the digestive tract might go unnoticed, and thus contribute to further malabsorption and failure to thrive. It is currently not clear whether or not the identification of low specific IgE to food allergens (sometimes a transient phenomenon without clinical expression) is a valid reason for the implementation of avoidance of such allergens in otherwise healthy infants, but in children with SBS, who usually have a deficient nutritional status, a trial of avoidance seems justified.

Extensively hydrolyzed formulas are widely used in children with cow's milk allergy, including those with SBS. Nevertheless, EH formulas are not completely safe for all allergic children (12), and better outcomes have been found in SBS children receiving elemental formula (2). The withdrawal of EH formula and its substitution by an elemental formula has led to dramatic clinical and physiologic improvements in children with SBS (1). The use of EH formula has been the general policy to prevent non-IgE allergy or intolerance to cow's milk in children with SBS, but, in view of the present results, we must wonder if another dietary management, such as elemental formula, is needed.

In summary, latex and food prevention measures should be mandatory in children with SBS. For the individual patient, food sensitization should be investigated, as it might be contributing as an added factor in the chronic diarrhea and malabsorption.

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