Prevalence of Latex-Specific IgE Antibodies in Atopic and Nonatopic Children With Type I Diabetes

THOMAS DANNE, MD
BODO NIGGEMANN, MD
BRUNO WEBER, MD, FRCPEDIN
ULRICH WAHN, MD

OBJECTIVE — The potential induction of allergic sensitization to latex from insulin vial tops stimulated an investigation of the prevalence of specific IgE antibodies to latex in serum and the relationship to atopic disease in children with diabetes.

RESEARCH DESIGN AND METHODS — In a cross-sectional study, serum samples of 112 children with type I diabetes (age: 15 [5–18] years; diabetes duration: 6 [1–14] years; median [range]) were investigated for total IgE, IgE screening for inhalational and nutritional allergens, and specific IgE antibodies to latex.

RESULTS — Specific IgE antibodies for inhalational and/or nutritional allergens was found in 42 (38%) children (atopic group). Seven children (6%) exhibited specific IgE antibodies (0.61 [0.40–3.84] kU/l) to latex in serum although none reported clinical symptoms of latex allergy. All latex-sensitized children were found in the atopic group. This prevalence of latex sensitization of 17% (7/42) in atopic children with diabetes is comparable with the frequency described in atopic children without diabetes. These seven patients had higher serum total IgE antibody levels (328 [113–1,000] kU/l) than atopic patients without latex sensitization ($n = 35$; 124 [24–857] kU/l; $P < 0.05$) or patients without atopy ($n = 70$; 33 [2–339] kU/l; $P < 0.001$). No differences in age or diabetes duration were observed between either group.

CONCLUSIONS — Sensitization to latex is found exclusively in children with atopic sensitization and appears to be related to atopic disease and not to frequent contact to latex through insulin injections. However, atopic patients may be at risk for reactions secondary to latex from insulin vials and syringes.

Latex allergy has become an increasingly recognized health problem. For those with diabetes, both insulin syringes and insulin vial stoppers contain latex and may therefore contribute to the development of latex allergy with potential—even life-threatening—allergic reactions (1). Two recent case reports describe clinically relevant local reactions secondary to insulin injections attributed to latex allergy in patients with diabetes (2,3). Therefore, proper identification of those patients likely to develop latex allergy is necessary. In such patients it may be important to minimize exposure to latex by using latex-free insulin vial tops and latex-free syringes (4). To gain information on the potential contribution of insulin injection procedures to the development of latex allergy, this study investigated the prevalence of latex sensitization and latex allergy in a representative group of children with type I diabetes.

RESEARCH DESIGN AND METHODS

— A cross-sectional study was performed. Aliquots of serum samples drawn for routine analyses in the diabetes outpatient clinic during a period of 6 months were collected. Since almost all children with diabetes in this area are sent to our outpatient clinic (5), the study population appears to be representative. Samples were analyzed for total IgE and specific IgE antibodies by a solidphase immunoassay, the Pharmacia CAP-system (KabiPharmacia, Uppsala, Sweden) (6). Inhalational (SX1) and nutritional (fx5) allergens were investigated by using the same automated IgE assay (7). SX1 contains the allergens timothy, birch, mugwort, house-dust mite, cat, dog, and *Cladosporium herbarum*. fx5 contains the food allergens milk, egg, fish, soy, wheat, and peanut. None of these allergens is known to cross-react with latex. The cutoff level of a positive specific IgE value is 0.35 kU/l. Patients able to develop specific IgE responses recognized by either SX1 or fx5 were defined as being atopic. Sensitized individuals with corresponding clinical symptoms were defined as allergic.

When patients proved to be positive for specific IgE to latex, a questionnaire was sent to their families. It contained questions on a general history of atopic disease (bronchial asthma, allergic rhinitis, or atopic dermatitis), clinical symptoms upon contact with latex in the daily environment (e.g., with balloons) and with medical equipment (e.g., during surgery).

The Mann-Whitney rank-sum test was used for nonparametric comparison between the groups with different sensitization results.

RESULTS

— A total of 70 out of 112 patients were negative for all tested allergens (62%, nonatopic group). Six patients tested positive for nutritional allergens, 25 for inhalational allergens, and 11 had a combined positivity for nutritional and inhalational allergens (total 42 [38%], atopic group). Seven of these (two inhalational allergen–positive, five mixed atopy) had specific IgE to latex ranging from 0.40 to 3.84 kU/l resulting in a prevalence of 17% (7/42) of latex-positive patients in the atopic group. No latex-positive patients were found in the nonatopic group. Age and diabetes duration were comparable in nonatopic and atopic patients (Table 1). Latex sensitization showed no association to older age or longer diabetes (age: 14 [11–18]; diabetes duration: 5 [1–9] years).

As expected, total IgE levels were significantly higher in the atopic than in the

From the Children's Hospital, Charité-Virchow-Clinic, Humboldt University, Berlin, Germany.
Address correspondence and reprint requests to Bodo Niggemann, MD, Children's Hospital, Charité-Virchow-Clinic, Humboldt University, Augustenburger Platz 1, 13353 Berlin, Germany. E-mail: tdanne@ukrv.de.
Received for publication 26 July 1996 and accepted in revised form 28 October 1996.

Downloaded from http://diabetesjournals.org/care/article-pdf/20/4/476/584312/20-4-476.pdf by guest on 28 February 2024

Table 1—*Prevalence of latex-sensitization and reported latex allergy in nonatopic and atopic children (with specific IgE to nutritional and/or inhalational allergens) with diabetes compared with atopic subjects without diabetes (11)*

	Nonatopic children with diabetes	Atopic children with diabetes	Atopic children without diabetes
n	70	42	306
Age (years)	14 (6–18)	15 (5–18)	6 (1–18)
Diabetes duration (years)	6 (1–14)	7 (1–14)	—
Sensitization to latex	0% (0/70)	17% (7/42)	21% (60/306)
Sensitized patients with anamnestic latex allergy	0% (0/0)	0% (0/7)	17% (9/53)

The rate of latex sensitization in the general population is 0.37% (8).

nonatopic group (Fig. 1). Interestingly, the latex-positive patients of the atopic group had significantly higher total IgE levels, compared with both the nonatopic and the atopic latex-negative patients (Fig. 1).

The questionnaire results revealed no clinical signs of latex allergy in any of the latex-sensitized patients. The number of previous surgical procedures was not unexpectedly high in this group (1 [0–3]). However, all latex-positive patients had clinical symptoms of atopic diseases, such as bronchial asthma, allergic rhinoconjunctivitis, or atopic dermatitis.

CONCLUSIONS — The present study indicates a high prevalence of sensitization to latex in children with diabetes (6%), when compared with the expected rate in the general population of 0.37% (8). Indeed, this high prevalence in children with diabetes corresponds to rates found in other high-risk populations such as hospital personnel with sensitizations between 11 and 21% (9,10). However, none of the seven patients with diabetes reported signs of clinical latex allergy (Table 1). This finding has to be confirmed by a latex provocation test, as the questionnaire approach may underestimate clinically manifest latex allergy (9,11).

The question arises whether this high prevalence of latex sensitization in children with diabetes may be related to the exposure to latex during insulin injection procedures. In a pediatric high-risk population for latex allergy, like children with spina bifida, the degree of latex sensitization correlates well with the number of operations (12). Therefore, in these children the degree of exposure to latex-containing material appears to be an important contributing factor for the development of latex allergy. In analogy to the situation in spina bifida, no association was found with diabetes duration, frequency of injections, or mode of insulin delivery (injections or pens).

Besides exposure to latex, atopic disease was a major risk factor for latex allergy in children with spina bifida (12). In this regard, it is of interest that 38% of the children with diabetes were sensitized to inhalational and/or nutritional allergens. This rate is considerably higher than expected in the background population (13). This is in agreement with a recent survey in Sweden (14), contradicting previous studies suggesting an even lower allergy rate in children with diabetes (15). Interestingly, the study in children with spina bifida also revealed a higher rate of atopy (41%) than expected (12).

It appears therefore, that the high rate of sensitization to latex in children with diabetes is secondary to the high rate of atopy in the study population. Indeed, all latex-positive subjects had specific IgE against nutritional and/or inhalation allergens. This finding is in keeping with the results of a large survey in atopic and nonatopic children (11). The prevalence rate of 17% in atopic children with diabetes in the present study corresponds well with the value of 21% in atopic children (11) (Table 1). The children with diabetes of the present study are considerably older than those without diabetes in the big survey (11). In spite of having more time for latex sensitization, however, the rate of latex sensitization was not higher.

In addition, serum total IgE as a marker of atopic disease was investigated. This supported the close association between atopy and sensitization to latex. Significantly higher total IgE levels were found in the latex-positive children with diabetes, even when compared with the atopic group (Fig. 1).

Further support for the importance of atopic disposition for latex sensitization comes from one family observed in the present study. This family has two children affected with diabetes and the nondiabetic mother has a clinically manifest latex allergy as well as bronchial asthma and allergic rhinoconjunctivitis. While the daughter with diabetes has both atopic disease and latex sensitization, the son with diabetes showed no latex sensitization and no clinical or biochemical evidence of atopic disease.

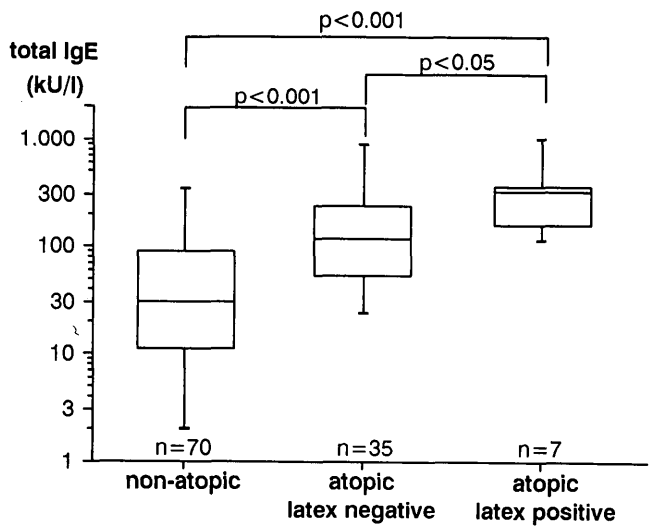

Figure 1—*Comparison of serum total IgE levels of children with type I diabetes with (atopic group) or without (nonatopic group) specific IgE to nutritional and/or inhalational allergens and sensitization to latex. Results are displayed as box plots where the upper and lower limits of the box represent the 25th and 75th centiles, the middle line represents the median, and the lines give the range.*

Downloaded from http://diabetesjournals.org/care/article-pdf/20/4/476/584312/20-4-476.pdf by guest on 28 February 2024

In conclusion, latex sensitization in children with diabetes appears to be secondary to atopic disease. Such was the case also in the two cases of clinical latex allergy described in patients with diabetes in the literature (2,3). This study provides no evidence for a contribution of the permanent exposure to latex via insulin injection procedures to the latex sensitization.

References

1. Vassallo S, Thurston TA, Kim SH, Todres DI: Allergic reaction to latex from stopper of a medication vial. *Anest Analg* 80:1057–1058, 1995
2. Towse A, O'Brien M, Twarog FJ, Braimon J, Moses AC: Local reaction secondary to insulin injection. *Diabetes Care* 18:1195–1197, 1995
3. MacCracken J, Stenger P, Jackson T: Latex allergy in diabetic patients (Letter). *Diabetes Care* 19:184, 1996
4. Bastyr EJ: Latex allergen allergic reaction (Letter). *Diabetes Care* 19:546, 1996
5. Danne T, Weber B, Hartmann R, Enders I, Burger W, Hövener G: Long-term glycemic control has a non-linear association to the frequency of background retinopathy in adolescents with diabetes: results from the Berlin Retinopathy Study. *Diabetes Care* 17:1390–1396, 1994
6. Axen R, Drevin H, Kober A, Yman L: A new laboratory diagnostic system applied to allergy testing (Abstract). *N Engl Reg Allergy Proc* 9:503, 1988
7. Eriksson NE: Allergy screening with Phadiatop and CAP Phadiatop in combination with a questionnaire in adults with asthma and rhinitis. *Allergy* 45:285–292, 1990
8. Moneret-Vautrin DA, Beaudouin E, Widmer S, Mouton C, Kanny G, Prestat F, Kohler C, Feldmann L: Prospective study of risk factors in natural rubber latex hypersensitivity. *J Allergy Clin Immunol* 92:668–677, 1993
9. Lagier F, Vervioet D, Lhermet I, Poyen D, Charpin D: Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* 90:319–322, 1992
10. Kaczmarek RG, Siverman BG, Gross TP, Hamilton RG, Kessler E, Arrowsmith-Lowe T, Moore RM: Prevalence of latex-specific IgE antibodies in hospital personnel. *Ann Allergy Asthma Immunol* 76:51–56, 1996
11. Liebke C, Niggemann B, Wahn U: Sensitivity and allergy to latex in atopic and nonatopic children. *Pediatr Allergy Immunol* 7:103–107, 1996
12. Michael T, Niggemann B, Moers A, Seidel U, Wahn U, Scheffner D: Risk factors for latex allergy in patients with spina bifida. *Clin Exp Allergy* 26:934–936, 1996
13. Hattevig G, Kjellman B, Björsten B, Johansson SGO: The prevalence of allergy and IgE antibodies to inhalant allergens in Swedish school children. *Acta Paediatr Scand* 76: 349–355, 1987
14. Stromberg LG, Ludvigsson GJ, Bjorksten B: Atopic allergy and delayed hypersensitivity in children with diabetes. *J Allergy Clin Immunol* 96:188–192, 1995
15. Villa MP, Cacciariari E, Bernardi F, Cicognani A, Salardi S, Zapulla F: Bronchial reactivity in diabetic patients. *Am J Dis Child* 142:726–729, 1988

Downloaded from http://diabetesjournals.org/care/article-pdf/20/4/476/584312/20-4-476.pdf by guest on 28 February 2024