

Latex allergy risk assessment in children and adolescents with type I diabetes mellitus

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An increased frequency of allergic reactions to latex has been reported in specific populations with chronic latex exposure. However, relevance of latex allergy to children and adolescents with type I diabetes mellitus (DM1) has not been studied yet. The aim of the study is to assess latex allergy risk in children and adolescents with DM1. Thirty-nine children with DM1 and 35 controls were enrolled. In a case-control study, we applied to all subjects a standard questionnaire, and specific Immunoglobulin E (IgE) concentrations for latex, common aeroallergens, and food-allergens were measured in serum samples. Latex exposure rates by means of medical procedures, operations, and latex glove usage were not different between DM1 and controls. Symptoms due to latex exposure were not determined in both groups. Three (7.7%) subjects in DM1 tested positive for latex-specific antibodies (LSIE), whereas no subject in controls. Diabetics that tested positive for latex-specific antibodies had the disease for three, 5 and 8 years. Nine (23.1%) of diabetics, and two (5.7%) of controls were atopic ($p = 0.04$). In our investigation, we found that children and adolescents with DM1 are not a risk group for latex allergy, and LSIE in children with DM1 was not accompanied by symptoms of latex allergy, or, presumably, increased risk of latex anaphylaxis.

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Latex allergy (LA) is one of the major health concerns of this century (1, 2). Rubber latex is a highly processed plant product derived from the tree, *Hevea brasiliensis*. It is widely used in medical, household, and various other areas. Latex is in two forms: natural rubber latex of which gloves and condoms are examples, and dry rubber latex products, which include vial stoppers, syringes plungers, and injection ports (3).

Rubber latex products can cause two types of allergic reactions (4). While most of the reactions are delayed type hyper-reactivity reactions that can cause irritant or allergic contact dermatitis, immunoglobulin E (IgE)-mediated immediate type reactions ranging from rhino-conjunctivitis, urticaria, angioedema, and asthma to fatal anaphylaxis reactions constitute the most important problem in LA (5).

The prevalence of LA in the general population is 1–6% (6, 7). Bernardini et al. (8) reported a very low prevalence of latex sensitization among the general pediatric population (0.7%; in 1175 children) with an absence of clinical symptoms to latex. Populations at high risk to develop LA are latex industry workers (10%), healthcare workers (8%–16%), and children with spina bifida or congenital urogenital abnormalities (20–68%), which are exposed to early and repeated latex exposure during the medical procedures or by instrumentation (8, 9). As hypersensitivity to latex has become an increasingly recognized problem in children, identification of all risk groups seems important to take preventive measures (9, 10).

Localized and systemic type I reactions to latex in syringes and insulin vial stoppers, in patients

with diabetes, have been documented in literature, as case reports (11–14). Primeau et al. (6) demonstrated that natural rubber vial stoppers release significant latex protein into solution during storage to elicit positive intradermal skin reactions in latex-allergic persons. During the study period, children and adolescents with type I diabetes mellitus (DM1) used insulin injections with syringes and insulin vial stoppers that contained latex. This continuous exposure to latex might contribute to the development of type I reactions to latex. Besides, all the children were hospitalized at least once because of diabetic ketoacidosis. During hospitalizations, insulin was administered with latex-containing syringes. In some chronic disease groups, for example in hemotologic-oncologic patients, latex sensitivity was found more than normal population because of increased latex exposure by latex-containing medical procedures or instrumentation (15). Consequently, a question rises if patients with DM1 might be another risk group for LA. Patients may be at risk of increased latex exposure because DM1 is also a chronic disease.

This study was conducted to compare the prevalence of latex-specific IgE (LSIE) in Turkish children with DM1 vs. a control population without DM1, and investigate risk assessment in children and adolescents with DM1 for latex reactions.

Material and methods

Ankara Training and Research Hospital Ethic Committee approved the investigational protocol described herein. Informed consent was obtained from all subjects or their parents.

Subjects

Two groups were constituted: children with DM1 and control group. The controls included healthy subjects, whom were chosen randomly; they were comparable for age and sex with the diabetic group. Type I diabetes group was formed from the patients, which were examined at the Pediatric Endocrinology Clinic during October 2003 and October 2004.

Protocol

A questionnaire was completed for all subjects. Allergy symptoms questions were prepared by benefiting from International Study of Asthma and Allergies in Childhood questionnaire (16). Personal allergic disease, family history of atopy, latex exposure by medical procedures or instru-

mentation, operations, latex glove, symptoms because of latex exposure (wheezing, itching, cough, watery eyes, sneezing, hives, or anaphylaxis), and atopy were sought (16). A subject was considered historically atopic if allergic rhinitis, rhino conjunctivitis, atopic dermatitis, or asthma were present; if acute nasal, ocular, or wheezing symptoms developed repeatedly on contact with dogs, cats, or house dust; or specific foods produced hives or oral allergy syndrome on multiple occasions. The same physician did both groups' physical examination and interviews.

Measurements

Serum samples were taken to analyze for total and specific IgE antibodies. Total IgE levels were analyzed with the nephelometry system (Biolateral, Spain). Specific IgE (sIgE) to latex was determined from the sera by the chemiluminescence's enzyme immunoassay system (Immulyte, Bio-DPC, CA, USA). Inhalant (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinea*, cat dander, mold mix, grass mix, weed mix, and tree mix) and nutritional (avocado, banana, chestnut, kiwi, melon, potato, strawberry, walnut, and food mix) allergens and latex were investigated by screening tests using the same automated IgE assay.

Patients who had positive specific IgE to latex without clinical symptoms were considered as sensitive to latex. The patients who also had clinical symptoms with latex exposure were diagnosed as allergic to latex (5).

Data analysis

A non-blinded, matched, case-control study was performed.

We compared: (i) the prevalence of LSIE and symptoms of LA in children and adolescents with DM1 with or without IgE to other environmental allergens (as an indicator of atopy) and (ii) the correlation of LSIE with LA and atopy in both groups.

Data analysis was performed with using spss for Windows 11.5. A p-value of <0.05 was regarded as significant. Fischer's exact test and Mann-Whitney *U*-test were used for statistical interpretation.

Results

Thirty-nine children and adolescents with DM1 and 35 controls were comparable with sex and age (Table 1). There was no significant difference between patients with DM1 and the controls for

Table 1. Characteristics of children and adolescents with type I diabetes mellitus and control groups

Characteristics	Type I diabetes mellitus group (n = 39)	Control group (n = 35)	p
Age (yr) median (min, max)	14 (5, 24)	16 (9, 24)	>0.05
Males (n)	16 (41%)	11 (31.4%)	>0.05
Females (n)	23 (59%)	24 (68.6%)	
Medical procedures or instrumentation (n)	3 (7.7%)	4 (11.6%)	>0.05
Operation (n)	5 (12.9%)	7 (20.1%)	>0.05
Latex glove usage (n)	3 (7.7%)	8 (22.9%)	>0.05
Family history of allergic disease (n)	17 (44.2%)	10 (29%)	>0.05
Personal history of allergic disease (n)	9 (23.4%)	9 (26.1%)	>0.05

medical procedures or instrumentation, operation, family and personal history of allergic disease (Table 1).

Among children and adolescents with DM1, five have been diagnosed < 1 yr ago. The duration of disease ranged between 0 and 12 yr (mean: 4.3, SD $\pm$ 3.6). Total hospitalization days in DM1 group were 7–153 days (mean: 45.7, SD $\pm$ 34.2).

Symptoms because of latex exposure (wheezing, itching, cough, watery eyes, sneezing, hives, or anaphylaxis) could not be determined in any subject in DM1 and controls.

Eosinophilia was detected in four patients (10.3%), and in one control (2.9%) ($p = 0.2$).

Total serum IgE levels ranged between 5.4–855 IU/ml (median: 41.8, mean: 109.7, SD: 169) in patients with DM1 and 4.2–619 IU/ml (median: 41.8, mean: 86 IU/ml, SD: 117.6) in the controls ($p = 0.9$). A total of 15.4% ($n = 6$) of DM1 and 8.6% ($n = 3$) of controls had high serum total IgE levels ($p > 0.05$).

Thirty DM1 and 33 controls were negative for all tested sIgE allergens (Table 2).

The prevalence of latex sensitivity in patients with DM1 was 7.7% ($n = 3$). In controls, no subject tested positive for latex. Compared with controls, the seroprevalence rate in children and

Table 3. Characteristics of three diabetic patients tested positive for latex-specific immunoglobuline E (IgE)

	Patient 1	Patient 2	Patient 3
Age (yr)	14	13	15
Sex	Girl	Girl	Girl
Duration of disease (yr)	3	5	8
Total hospitalization days	44	15	60
Family history of allergic disease	Asthma	None	Drug
Personal history of allergic disease	None	Allergic rhino conjunctivitis	None
History of latex exposure by medical procedures, operations and latex glove	None	None	None
Positive sIgE for nutritional allergens	No	Yes	No
Positive sIgE for inhalational allergens	Yes	Yes	Yes
sIgE for latex (IU/ml)	0.60	100	0.40
Total IgE (IU/ml)	25.7	484	125.8

adolescents with DM1 for latex was not significantly higher ($p > 0.05$).

The mean duration of the disease in latex-positive patients with DM1 when compared with negative ones was slightly longer (5.3 vs. 4.6 yr), but showed no statistical difference ($p > 0.05$). None of the three latex-positive DM1 patients had a history of medical procedures or instrumentation, operation or latex glove usage. There was no statistical significance between latex-positive and -negative subjects according to history of medical procedures ($p > 0.05$). These three patients also showed positive sIgE results for other inhalant and/or nutritional allergens (Table 3).

Eleven subjects in study group were considered as atopic (14.9%). Nine (23.1%) were in DM1 patients, and two (5.7%) were in controls. Atopy rate in children and adolescents with DM1 was higher than controls ($p = 0.04$).

Three latex-sensitized patients with DM1 were offered latex-free syringes. Besides, to eliminate the exposure to latex, they were advised to use non-latex gloves during housework. They were also advised that their partners should not use condoms when they are sexually active, in the future. After a 3-yr follow-up, these three girls with DM1 did not develop LA symptoms. They told that they obeyed our suggestions, completely. They are using latex-free insulin syringes.

Discussion

This study is a comparative data on investigation risk assessment in children and adolescents with DM1 for latex reactions.

Our patients with DM1 were frequently hospitalized. That might have caused increased latex exposure compared to normal population. Type I diabetes is a chronic illness and our

Table 2. Positive specific immunoglobulin E (sIgE) test results for children and adolescents with type I diabetes mellitus and controls

	Children and adolescents with type I diabetes mellitus (n = 39)	Controls (healthy subjects) (n = 35)	p
All specific IgEs (n)	9 (23.1%)	2 (5.7%)	0.04
Nutritional allergens (n)	4 (10.3%)	1 (2.9%)	>0.05
Inhalational allergens (n)	8 (20.5%)	1 (2.9%)	0.02

patients were frequently hospitalized which might have caused increased latex exposure compared to normal population. In addition, they were using latex-containing instrumentations to administer insulin during the study period.

Case reports of type I LA reactions, by insulin injections, in DM1 patients were reported in literature. Sources of latex were identified as plungers in insulin syringes and stoppers used for insulin bottles. These cause continuous exposure to small amounts of latex in every injection (11–14).

Increased latex exposures by surgical and invasive procedures with latex-containing devices have been identified in some chronic disease groups (5, 10, 15, 17, 18).

In this study, we aimed to assess the risk for LA in children and adolescents with DM1. We compared medical procedures, operations, and latex glove usage with controls, and we found no differences between DM1 and controls. In addition, there were no significant differences between DM1 group and the controls between family and personal history of allergic disease and none of the subjects in the study population showed allergic reactions to latex.

The prevalence of latex sensitivity was 7.7% (3/39) in children with DM1, and was not accompanied by symptoms of LA. Our result was similar with Danne et al. (19) whom reported the prevalence of LSIE in 112 children and adolescents with DM1 as 6%, and none had clinical symptoms of LA.

Autoimmune disorders are considered to be associated with a Th1 immune response while allergic diseases with a Th2 response (20). The Th1 and Th2 response controls the development of the same subset and suppresses the effector cells of the other subset. Therefore, it has been suggested that allergic diseases and DM1 are mutually exclusive and unlikely to be present in the same individual. Caffarelli et al. (20) investigated the frequency of atopic allergic diseases in children with DM1 in comparison with a general population. They found that allergic diseases in atopic children were not inversely associated with DM1 and IgE sensitization was similar to that of general population. Atopy and DM1 may exist in the same individual. Genetic and environmental factors might be responsible for this. The incidence of DM1 and allergic disease are both increasing. Common environmental factors might be responsible for this such as reduced exposure to infections that may alter immune system to determine individual susceptibility to both allergic diseases and DM1.

Atopy is an important risk factor in allergic reactions to latex. In this study, atopy prevalence was 23.1% (9/39) in patients with DM1, whereas it was 5.7% (2/35) in controls ($p = 0.04$). All of the three LSIE-positive children with DM1 were atopic. Danne et al. (19) observed latex sensitization exclusively in atopic children with DM1. They concluded that latex sensitization is related to atopy but not to contact to latex through insulin injections. We also observed that LSIE in children with DM1 was correlated with atopy.

We consider that, if recently diagnosed children and adolescents with DM1 are atopic, healthcare workers following them should be careful to use latex-free insulin vials and syringes.

Although our study has a case-control design, the major limitation is the small number of subjects, which does not give enough statistical power to it. Furthermore, some studies (19) have already shown the finding of LA in atopic and non-atopic children with DM1. However, risk assessment for LA in children and adolescents with DM1 was not investigated before. In our investigation, we found that LSIE in children with DM1 was not accompanied by symptoms of LA, or, presumably, increased risk of latex anaphylaxis. We confirmed that diabetics, at risk for reactions secondary to latex from insulin vials and syringes, when latex sensitized, are not a risk group for latex sensitization.

References

1. MEADE BJ, WEISMANN DN, BEEZHOLD DH. Latex allergy: past and present. *Int Immunopharmacol* 2002; 2: 225–38.
2. TURJANMAA K, ALENUS H, REUNALA T, PALOSUO T. Recent developments in latex allergy. *Curr Opin Allergy Clin Immunol* 2002; 2: 407–12.
3. KANDEEL A, AKL M. Latex allergy. *Pediatr Asthma Allergy Immunol* 1999; 13: 1–14.
4. KURUP VP, FINK JN. The spectrum of immunologic sensitization in latex allergy. *Allergy* 2001; 56: 2–12.
5. GULBAHAR O, DEMIR E, METE N, et al. Latex allergy and associated risk factors in a group of Turkish patients with spina bifida. *Turk J Pediatr* 2004; 46: 226–31.
6. PRIMEAU MN, ADKINSON F, HAMILTON R. Natural rubber pharmaceutical vial closures release latex allergens that produce skin reactions. *J Allergy Clin Immunol* 2001; 107: 958–62.
7. JORGE A, LORENTE F, TABORDA-BARATA L. Prevalence of latex sensitization and allergy in Portuguese children. *Pediatr Allergy Immunol* 2006; 17: 466–73.
8. BERNARDINI R, NOVEMBRE E, INGARGIOLA A. Prevalence and risk factors of latex sensitization in an unselected pediatric population. *J Allergy Clin Immunol* 1998; 101: 621–5.
9. BODE CP, FULLERS U, RÖSELER S, WAWER A, BACHERT C, WAHN V. Risk factors for latex hypersensitivity in childhood. *Pediatric Allergy Immunol* 1996; 7: 157–63.

10. BOSTANCI I, YILMAZ R, DALLAR Y, TANYER G. Latex sensitivity in hematologic and oncologic non-atopic pediatric patients. *Pediatr Asthma Allergy Immunol* 2003; 16: 117–20.
11. HOMAN RP. Latex hypersensitivity in a child with diabetes. *Arch Pediatr Adolesc Med* 2000; 154: 281–2.
12. MACCRACKEN J, STENGER P, JACKSON T. Latex allergy in diabetic patients. *Diabetes Care* 1996; 19: 184.
13. J.BASTYR EJ III Latex allergen allergic reactions. *Diabetes Care* 1996; 19: 546.
14. ROEST MA, SHAW S, ORTON DI. Insulin-injection site reactions associated with type I latex allergy. *N Eng J Med* 2003; 348: 265–6.
15. BOSTANCI I, TÜRKTAŞ I, EROL I, KIROĞLU G. Prevalence of latex sensitivity in patients with malignancies. *J Invest Allergol Clin Immunol* 2001; 11: 271–4.
16. ASHER MI, KEIL U, ANDERSON HR, et al. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur R J* 1995; 8: 483–91.
17. NUCERA E, SCHIAVINO D, POLLASTRINI E, et al. Sublingual desensitization in children with congenital malformations and latex allergy. *Pediatr Allergy Immunol* 2006; 17: 606–12.
18. PAMIES R, OLIVER F, RAULF-HEIMSOTH M, et al. Patterns of latex allergen recognition in children sensitized to natural rubber latex. *Pediatr Allergy Immunol* 2006; 17: 55–9.
19. DANNE T, NIGEMANN B, WEBER B, WAHN U. Prevalence of latex-specific IgE antibodies in atopic and nonatopic children with type I diabetes. *Diabetes Care* 1997; 20: 476–8.
20. CAARELLI C, CAVAGNI G, PIERDOMENICO R, CHIARI G, SPATTINI A, VANELLI M. Coexistence of IgE-mediated allergy and type I diabetes in childhood. *Int Arch Allergy Immunol* 2004; 134: 288–94.