

The Evaluation of Latex Allergy with Skin Prick Tests in Children with Meningomyelocele

Meningomyeloselli Çocuklarda Lateks Allerjisinin Deri Prick Testi ile Değerlendirmesi

Dilek Yılmaz¹, Akın Soner Amasyalı², Yasin Bulut³, Mehmet Şirin Kaya³, Ferah Sönmez⁴, İmran Kurt Ömürlü⁵, Berna Gültekin Korkmazgil⁶, Ayşe Yenigün⁷

¹ Assoc.Prof.Dr., Depart. of Pediatric Nephrology, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

² Med.Dr., Depart. of Urology, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

³ Med.Dr., Depart. of Pediatrics, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

⁴ Prof.Dr., Depart. of Pediatric Nephrology, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

⁵ Prof.Dr., Depart. of Biostatistics, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

⁶ Prof.Dr., Depart. of Medical Microbiology, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

⁷ Prof.Dr., Depart. of Pediatric Allergy, Aydın Adnan Menderes University School of Medicine, Aydın, Turkey

Summary

Objective: Latex allergy and its clinical presentation are rising in prevalence across the globe, especially among patients with meningomyelocele (MMC) and patients on dialysis. The aim of the study was to evaluate the role of diagnostic procedures and nonsurgical treatments in latex sensitization; as well as to investigate latex allergy in patients with MMC and patients undergoing dialysis.

Material and Method: Forty children with MMC who were or were not undergoing dialysis were included in the study. A questionnaire was administered, and latex specific IgE serum determination was performed for each. All children underwent skin prick tests (SPTs) using latex solutions, house dust mites and commonly cross-reacting food allergens.

Results: The mean age of the patients was 8.6±4.3 (1-17) years. The SPT results showed that 2.5% of the patients tested positive for latex allergy and the results of the testing for latex-specific IgE were positive in 2.5% of the patients, as well. Atopy (i.e., positive SPT to house dust mites) was present in 1 (2.5%) patient. Although the number of surgical procedures was significantly higher in the patients who had shunts; no significant relationship between the presence of a shunt and latex sensitization was observed.

Conclusion: Lower latex allergy rate, compared to previous data in patients with MMC, was found. However it was not as low as the rate reported in the general population. The use of latex-free gloves in all procedures performed in these cases, nonlatex polyvinyl chloride catheters in clean intermittent catheterization and ordinary nonballoon tips in barium enemas could decrease the risk of sensitization.

Key words: Clean intermittent catheterization, latex sensitization, meningomyelocele, skin prick test

Özet

Amaç: Lateks allerjisi prevelansı, özellikle meningomyelosel (MMS) ve diyalize giren hastalarda tüm dünyada artmaktadır. Bu çalışmada, lateks duyarlılığında tanısıl prosedürler ve cerrahi olmayan tedavilerin değerlendirilmesi, aynı zamanda MMS ve diyalize giren hastalarda lateks allerjisinin araştırması amaçlandı.

Gereç ve Yöntem: Diyalize giren veya girmeyen, 40 MMS tanılı, çocuk hasta çalışmaya dahil edildi. Her hastaya anket dolduruldu ve lateks spesifik serum IgE tayini yapıldı. Lateks solüsyonu, ev tozu akarları ve sıklıkla çapraz reaksiyon veren besin allerjenleri kullanarak, tüm hastalara prick deri testi (PDT) uygulandı.

Bulgular: Hastaların ortalama yaşları 8.6±4.3 (1-17) idi. Hastaların %2.5'inde PDT lateks allerjisi için pozitif saptandı. Lateks spesifik serum IgE düzeyi de, %2.5 hastada pozitif bulundu. Atopi (ev tozu akarları pozitif

PDT) bir hastada (%2.5) vardı. Şanti olan hastalarda, geçirilmiş cerrahi işlem sayısı anlamlı olarak fazla olsa da, lateks duyarlılığı ile şant varlığı arasında ilişki bulunmadı.

Sonuç: Çalışmada, daha önceki yayınlara göre, MMS hastalarında düşük oranda lateks allerjisi saptandı. Fakat, bu oran genel popülasyondaki kadar düşük değildi. Cerrahi işlemlerde lateks içermeyen eldivenlerin kullanımının, temiz aralıklı kateterizasyon sırasında nonlateks polivinil klorid kateterlerin kullanımının ve baryum enema işlemlerinde sıradan balon içermeyen uçların kullanımının duyarlılık riskini azaltabileceği düşünülmektedir.

Anahtar kelimeler: Temiz aralıklı kateterizasyon, lateks duyarlılığı, meningomyelosel, prick deri testi

Kabul Tarihi: 28.Eylül.2019

Introduction

It is well known that the incidence of latex allergy is increasing; especially in dialysis patients with spina bifida. Previous studies reported a 9.7-73% prevalence of latex allergy in spinal dysraphism (SPD) patients (1,2). In a more recent study from Turkey the prevalence was found to be 4.3-10.8% (3). However, latex allergy affects only 0.3-0.7% of the general pediatric and adult population (4). Clinically latex allergy manifests as contact urticaria, erythema, edema and urticarial plaques caused by a type 1 hypersensitivity reaction. Manifestations may remain localized or progress to a systemic reaction, such as anaphylaxis (5).

Causative risk factors for latex allergy include a genetic predisposition for type 1 hypersensitivity reactions, increased specific IgE levels and continuous exposure. Patients undergoing multiple operations, patients use latex containing catheters and healthcare workers are at risk for latex allergy (6).

Currently, however, the use of latex containing catheters is limited in most of the clinics. It was assumed that the prevalence of a latex allergy in these patients would be low. Thus; it was aimed to investigate the incidence and risk factors of latex allergy in meningomyelocele (MMC) patients who required clean intermittent catheterization (CIC) and dialysis patients. Skin prick tests were administered to each patient and data were compared with previously published data to determine if the incidence of latex allergy would or would not decrease over time.

Material and Method

This study was approved by the institutional ethics committee of Adnan Menderes University. (Approval#: 2013/12). Forty spina bifida patients who were followed in Adnan Menderes University pediatric nephrology clinic, who required CIC, who were or were not undergoing dialysis and who were treated in the pediatric nephrology outpatient clinic between 2001 and 2013 were enrolled in the study. Informed consent for each patient was obtained from their parents. Patients between the ages of 1-18 who were included in the study were given a questionnaire about the clinical characteristics of, risk factors for and presence of atopy.

Blood samples were drawn, and serum specimens were stored at -20 °C after degradation. Serum samples were sent to an external private laboratory (Duzen Lab) for latex specific IgE analysis by cold chain compliance. Tests were performed by latex specific IgE kits, and a chemiluminescence method was used with the Immulite 2000 (Siemens Healthcare Diagnostic, Erlangen, Germany) device.

The results were organized into 7 classes: <0.35 kU/L Class 0 (negative), 0.35-0.69 kU/ml Class I (very low), 0.70- 3.49 kU/L Class II (low), 3.50-17.49 kU/L Class III (mild), 17.50-52.49 kU/L Class IV (moderate), 52.5-99.99 kU/L Class V (high) and >100 kU/L Class VI (very high).

All children underwent skin prick tests (SPTs) using a latex solution that included latex and aeroallergens (Olea europea, horse chestnuts, Dermatophagoides farinae, Dermatophagoides pteronyssinus) and four common food

allergens (strawberry, eggs, tomatoes, and cow's milk). A standard allergen extract panel (Stallergenes, France) and comprised histamine and saline controls (positive and negative controls, respectively) were applied to the volar surface of the forearm of each patient. It was confirmed that the patients had not used nonsteroidal anti-inflammatory, antihistaminic, decongestant or immunosuppressive drugs before the skin test. Patients who had infections and parasites were excluded from the study. Materials required for an anaphylactic reaction were kept on hand in case of an emergency.

The skin prick test results were described previously (7); no erythema, induration or pseudopod: negative reaction; erythema <21 mm: +1; erythema >21 mm: +2; induration without erythema and pseudopod: +3; and induration with erythema and pseudopod: +4.

Descriptive statistics are presented as the mean $\pm$ SD and the median (25th–75th percentiles) where appropriate. Spearman's correlation analysis was used to evaluate the correlation between variables. P-values <0.05 were considered to be statistically significant.

Results

A total of 40 patients were enrolled in this study and 52.5% were male. The mean age of the patients was 8.6 ± 4.3 years. Eighty percent of the patients (n=32) had surgery for myelomeningocele; 7.5% of the patients (n=3) received peritoneal dialysis treatment; 7.5% of the patients (n=3) received hemodialysis; and 5% of the patients (n=2) had both surgery for myelomeningocele and underwent peritoneal dialysis with applying CIC (Table 1).

The median age at the time of the first operation was (25-75 p) 1.5 (1-33) months; the median age of CIC initiation was (25-75 p) 42 (12-60) months (Figure 1); and the median duration of CIC was (25-75 p) 24 (12-48) months. The mean number of operations for each patient was 3.2 ± 1.5 and a voiding cystourethrogram was conducted in 17.5% of patients 3 or more times. An allergy history was noted in 40% of the patients, 15% of their mothers, 12.5% of their fathers and 15% of their brothers.

Figure 1. The beginning time of clean intermittent catheterization

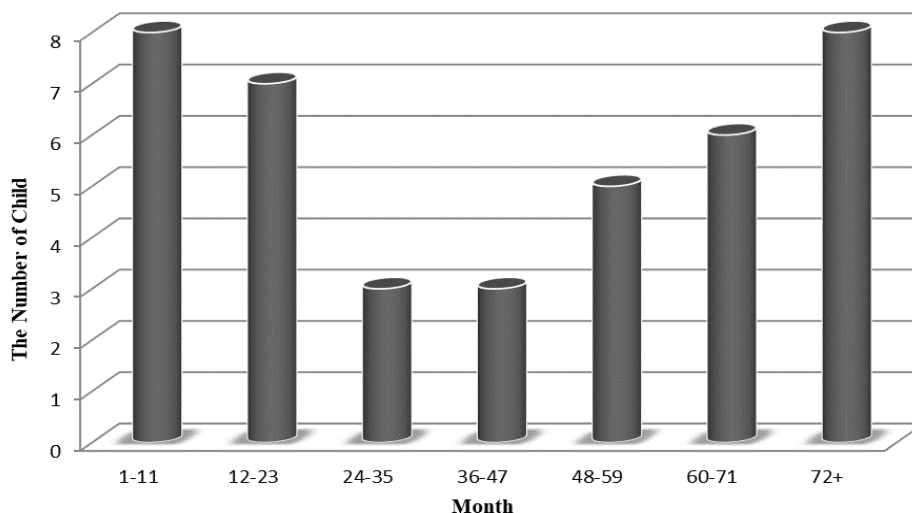


Table 1. The features of all groups

	Meningomyelocele (n=32)	Peritoneal Dialysis (n=3)	Hemodialysis (n=3)	Meningomyelocele + Peritoneal Dialysis (n=2)
Age (y)	8.0±4.5	10.5±3.2	11.6±1.5	11.5±3.5
Gender (F/M)	16/16	1/2	0/3	2/0
Serum latex-specific I (kU/L)				
median	0.09	0.09	0.09	50
(25th-75th percentiles)	(0.09-0.09)	(0.09-0.09)	(0.09-0.09)	(0.09-50)
Latex SPT				
negative	21	3	3	0
+1	8	0	0	0
+2	3	0	0	1
+3	0	0	0	1
+4	0	0	0	0

No correlations were found between allergy history and the age of CIC initiation, peritoneal dialysis or hemodialysis, the number of urodynamic tests and the existence of a ventriculoperitoneal shunt ($p>0.05$). Additionally; there was no significant difference in allergy history detected between the patients that underwent an operation more than 4 times and the patients that underwent an operation fewer than 4 times (40% for each). Latex allergy history was not reported in any of the patients or their families.

Any life-threatening complications were not seen during the skin tests. Additionally; any food allergies were not identified with the skin prick tests. However; +, ++, +++ induration were detected in 20%, 10%, and 2.5% of patients, respectively. In one case of positive induration, both a peritoneal dialysis catheter and a ventriculoperitoneal shunt catheter were in place simultaneously. The results of testing for latex-specific IgE were positive in only 1 (2.5%) patient. Latex-specific IgE levels were as follows: <0.1 kU/L in 87.5%, 0.10-0.34 kU/L in 5%, 0.35-0.69 kU/L in 2.5%, 0.7-3.49 kU/L in 2.5% and >100 kU/L in 2.5% of the patients. Latex-specific >100 kU/L IgE levels were detected in one patient who had the +++ skin prick test. Latex-specific IgE levels showed no correlation with the above mentioned clinical characteristics and no association was found between latex-specific IgE levels and skin prick test results.

Positive prick latex tests were correlated with the age of CIC initiation ($p=0.031$, $r=0.341$). In addition, a significant correlation was found between the mean frequency of CICs per day and the age at the time of the first operation ($p=0.013$, $r=-0.388$), the number of voiding cystourethrograms ($p=0.001$, $r=0.520$) and the age of CIC initiation ($p=0.002$, $r=0.474$). Furthermore; in one case, +++ induration was detected against *D. farinea* in a skin prick test.

Discussion

This study revealed that the incidence of latex allergy was low in patients with MMC compared with past studies with a similar study population. However; it was still higher than the incidence of latex allergy in the general population. In this study, skin prick tests were used along with serum specific IgE concentrations to evaluate the incidence of latex allergy. It has been demonstrated that denatured allergens are included in the serologic tests; so the sensitivity of a prick test is higher than the sensitivity of serum specific IgE concentrations for the diagnosis of a latex allergy (90-98% vs 84-86%) (8). Nevertheless; Schuler et al. provided strong evidence that a latex allergy cannot be excluded by a skin prick test because the prick-test-solution contains latex-proteins Hev b1, 3, 5, and 6, but not Hev b8, which is used to diagnose a latex

allergy from elevated specific IgE concentrations (9). Increased latex specific IgE concentrations were found in only one patient in this cohort.

Natural latex products cause 2 types of allergic reactions; type I immune reactions, which are mediated by IgE and type IV late onset hypersensitive reactions (10). Latex itself never causes type IV hypersensitive reactions but latex products containing chemical preservative substances can lead to late onset hypersensitivity. Atopy may also increase the risk of latex allergy by 4.4-25 fold and atopy has been reported in up to 67% of patients with a latex allergy (11). Recently; Chua et al. reported a 46% latex allergy prevalence in spina bifida patients and a strong relationship between latex sensitization and atopy (12).

Reports of latex allergic reactions have increased in recent years. This may be due to increased exposure to materials containing latex, especially among at-risk patients undergoing multiple operations, as well as the use of latex containing catheters by patients and latex gloves by healthcare workers (13). Limiting latex exposure may prevent latex allergy (14). In accordance with this hypothesis, a low incidence of latex allergy was found in patients with MMC who use latex-free catheters. However; the incidence was still higher in patients with MMC than in the normal population. Therefore; it was assumed that patients with MMC may have a propensity for latex allergy. Consistent with this, Szepefalusi et al. surmised that spinal dysraphism patients are more prone to latex allergy (15). Another study revealed that the disease-associated susceptibility is independent of the number and duration of operations that the patient has undergone (3). In a recent study, a low latex allergy rate was reported in spinal dysraphism patients that was comparable with that of a control group (3% vs 1.7%). However, the control group in their study was selected from patients who were referred for evaluation of allergic diseases. The authors stated that a low number of surgeries or a disease-associated susceptibility with a geographically variable genetic association may affect latex sensitization (16). Moreover; Rihs et al. emphasized that genetic

susceptibility to latex allergy may vary in different geographic distinctions with respect to IgE responsiveness to latex and HLA class 2 antigens DR4 and DQ8 (17). However, when the results of the study were compared with those of previous studies from Turkey (3), the incidence of latex allergy decreased from 4.3% to 2.5% in the same geographic region. It was proposed that the use of latex-free catheters and the low number of operations may have caused a lower latex allergy incidence.

In another study; Yeh et al. reported an observed clinical latex allergy prevalence of 23.2% in patients with MMC, and they found that multiple operations under anesthesia led to a higher risk of clinical latex allergy (6). In accordance with the results of this study, recently published data showed that a history of 4 or more operations seemed to be the most important risk factor for latex sensitization (18). On the other hand; Majed et al. found 30% positivity for latex allergy in 73 MMC patients using skin prick tests (14). In contrast; Eiwegger et al. indicated that CIC was not a risk factor for a latex allergy and that there was a disease-associated propensity that existed for latex sensitization (19). However, it is believed that CIC is a potential risk factor for latex allergy and that CIC promotes sensitization during mucosal contact (20).

Conclusion

This current study has some drawbacks, including a limited number of patients and a lack of a control group. However; study results were compared with previous data and showed a lower latex allergy rate; although, it was not as low as the rate found in the general population. It was supposed that using latex-free gloves in all procedures and nonlatex polyvinyl chloride catheters in CICs could prevent latex sensitization. However, it is not fully understood how the propensity for and genetic susceptibility to the disease itself lead to latex sensitization in patients with MMC.

Declaration of Interest: The authors report no conflicts of interest

"This study was supported by Aydın Adnan Menderes University Scientific Research Project Commission (TPF-14010)."

References

1. Capriles-Hulett A, Sanchez-Borges M, Von-Scanzoni C, Medina JR. Very low frequency of latex and fruit allergy in patients with spina bifida from Venezuela: influence of socioeconomic factors. *Ann Allergy Asthma Immunol* 1995;75(1):62-4.
2. Kelly KJ, Kurup VP, Reijula KE, Fink JN. The diagnosis of natural rubber latex allergy. *J Allergy Clin Immunol* 1994;93(5): 813-6.
3. Gulbahar O, Demir E, Mete N, Ulman I, Can D, Sin A, et al. Latex allergy and associated risk factors in a group of Turkish patients with spina bifida. *Turk J Pediatr* 2004;46(3):226-31.
4. Liebke C, Niggemann B, Wahn U. Sensitivity and allergy to latex in atopic and non-atopic children. *Pediatr Allergy Immunol* 1996;7(2):103-7.
5. Laxenaire MC, Mertes PM. Anaphylaxis during anaesthesia. Results of a twoyear survey in France. *Br J Anaesth* 2001;87(4):549-58.
6. Yeh WS, Kiohara PR, Soares IS, Carmona MJ, Rocha FT, Galvao CE. Prevalence of sensitivity signals to latex in meningomyelocele patients undergoing multiple surgical procedures. *Rev Bras Anesthesiol* 2012;62(1):56-62.
7. Carr WW. Improvements in skin-testing technique. *Allergy Asthma Proc* 2006;27(2):100-3.
8. Blanco C, Carrillo T, Ortega N, Alvarez M, Dominguez C, Castillo R: Comparison of skin-prick test and specific serum IgE determination for the diagnosis of latex allergy. *Clin Exp Allergy* 1998;28 (8):971-6.
9. Schuler S, Ferrari G, Schmid-Grendelmeier P, Harr T. Microarray-based component-resolved diagnosis of latex allergy: isolated IgE-mediated sensitization to latexprofilin Hev b8 may act as confounder. *Clin Transl Allergy* 2013;28;3(1):11.
10. Kenneth T Kim, Ghassan S. Safadi, Khalid M Sheikh. Diagnostic evaluation of type I latex allergy. *Ann Allergy Asthma Immunol* 1998;80(1):66-70.
11. Garcia JA. Type I latex allergy: a follow-up study. *J Investig Allergol Clin Immunol* 2007;17(3):164-7.
12. Chua X, Mohamed J, van Bever HP. Prevalence of latex allergy in spina bifida patients in Singapore. *Asia Pac Allergy* 2013;3(2):96-9.
13. Agarwal S, Gawkrödger DJ. Latex allergy: a health care problem of epidemic proportions. *Eur J Dermol* 2002;12(4):314-5.
14. Majed M, Nejat F, Khashab ME, Tajik P, Gharagozloo M, Baghban M et al. Risk factors for latex sensitization in young children with myelomeningocele. *Clinical article. J Neurosurg Pediatr* 2009;4(3):285-8.
15. Szepefalusi Z, Seidl R, Bernert G, Dietrich W, Spitzauer S, Urbanek R. Latex sensitization in spina bifida appears disease-associated. *J Pediatr* 1999;134(3):344-8.
16. Goldberg H, Aharony S, Levy Y, Sivan B, Baniel J, Ben Meir D. Low prevalence of latex allergy in children with spinal dysraphism in non-latex-free environment. *J Pediatr Urol* 2016;12(1):52.e1-5.
17. Rihs HP, Chen Z, Rueff F, Cremer R, Raulf-Heimsoth M, Baur X, et al. HLA-DQ8 and the HLA-DQ8-DR4 haplotype are positively associated with the hevein-specific IgE immune response in health care workers with latex allergy. *J Allergy Clin Immunol* 2002;110(3):507-14.
18. Bueno de Sa A, Camilo Araujo RF, Cavaleiro S, Carvalho Mallozi M, Sole D. Profile of latex sensitization and allergies in children and adolescents with myelomeningocele in Sao Paulo, Brazil. *J Investig Allergol Clin Immunol* 2013;23(1):43-9.
19. Eiwegger T, Dehlink E, Schwindt J, Pomberger G, Reider N, Frigo E, et al: Early exposure to latex products mediates latex sensitization in spina bifida but not in other diseases with comparable latex exposure rates. *Clin Exp Allergy* 2006;36(10):1242-6.
20. Pires G, Morais-Almeida M, Gaspar A, Godinho N, Calado E, Abreu-Nogueira J, et al: Risk factors for latex sensitization in children with spina bifida. *Allergol Immunopathol (Madr)* 2002;30(1):5-13.

Correspondence:

Assoc.Prof.Dr. Dilek Yılmaz

Aydın Adnan Menderes University, School of Medicine, Department of Pediatric

Nephrology, 09100, Aytepe, Aydın /Turkey

Tel: +90.505.5954374

E-mail: dr.dlkylmz@gmail.com