Sensitivity to Rubber Chemicals and Latex Among Hemodialysis Patients

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Sir,

Patients undergoing chronic hemodialysis can, although rarely, develop hypersensitivity reactions to substances used in dialysis equipment (1, 2). The aim of our study was to evaluate the frequency of latex and rubber chemical hypersensitivity in patients undergoing long-term hemodialysis.

PATIENTS AND METHODS

We enrolled 154 consecutive hemodialysis patients (66 women and 88 men). The median time of dialysis was 53±44 months, with a range of 1–205 months. Skin-prick tests were performed with a standardized commercial extract of non-ammoniated latex (Stallergènes, Paris, France) and with glove extracts prepared as previously reported (3). Briefly, twenty 1 cm^2 (400 mg total weight) freshly cut glove pieces (Le Petit, Gradate, Como, Italy) were incubated for 30 min in 5 ml of sterile 0.9% NaCl saline solution. The incubation fluid was used as a stock solution for prick testing. Histamine hydrochloride (10 mg/ml) and 0.9% NaCl saline solution served as positive and negative controls, respectively. Wheals of 3 mm or greater were regarded as positive in the absence of a reaction to saline. A glove user test was performed as follows: a fingertip was cut from a surgical glove, dampened with water, and placed on one finger for 15–30 min. If the reaction was negative, the whole glove was worn for the same amount of time. One vinyl glove was used as control. Urticaria on the finger/hand exposed to latex was regarded as a positive reaction. Only 83 patients accepted to undergo the patch test. These tests were performed with a series of 32 rubber additives (4). The allergens were applied in Finn Chambers with Scampor tape to each patient's back. Readings were taken after 2 and 4 days. The reactions were scored in accordance with the recommendations of the International Contact Dermatitis Research Group. Any drug that could have interfered with the allergic tests was stopped at least 2 weeks prior to testing. Laboratory evaluation included measurement of total IgE level by the PRIST (Pharmacia, Uppsala, Sweden) and serum-specific IgE to latex by a fluorescence enzyme-linked immunoassay (CAP-FEIA system; Pharmacia). The threshold of positivity for the CAP test was set at 0.35 kU/l. Atopy was assessed by a careful clinical history of atopic dermatitis and/or seasonal or perennial rhinitis or asthma, and by increased IgE levels. Informed consent was given by subjects prior to participation in the study.

Statistical analysis of data was performed by two-tailed chi-squared test and Fisher exact test when necessary. Mean values of continuous variables were compared using Student's *t*-test. Probability (p) values less than 0.05 were considered significant.

RESULTS

Mean patient age was 55.8 (±12.9) years. Among the 154 hemodialysis patients, atopy was found in 8 (5.2%), while 23 (15%) had previous or present dermatitis and 64 (41.5%) pruritus. Only one patient (0.6%) had latex allergy. This patient, a 60-year-old woman, had the only positive clinical history after latex exposure during the hemodialysis treatment, mostly when touching gloves. The symptoms of contact urticaria occurred within minutes of contact with latex and included itching, redness and wheals on the skin at the site of contact. She also presented a positive SPT for latex, a positive use test, and a positive CAP to latex (6.22 kU/l). By history, the latex allergy was induced by hemodialysis. She did not manifest dermatitis or pruritus, nor a history of atopy. None of the other subjects had latex sensitivity based on skin tests or CAP.

Eighty-three patients (53.9%) accepted to undergo the patch test. A history of atopic disease was reported by 6 subjects (7.2%), pruritus by 35 (42.2%) and dermatitis by 22 (26.5%). Sixteen patients (19.3%), exhibited positive patch tests to rubber antigens (Table I). For 9 of them, the rubber allergy was considered clinically relevant, as these patients had previously had episodes of allergic contact dermatitis following exposure to the rubber allergens. However, it was not possible to assess whether the sensitivity to the rubber chemicals was induced by hemodialysis or prior to treatment. The most common sensitizers were thiuram mix (12 cases) and carba mix (5 cases) We did not find any significant differences concerning age, sex, duration of hemodialysis, history of atopy, prior or current pruritus among patients with either positive or negative patch tests (Table I). Statistical analysis showed, however, a significant association between positive patch test results and the presence of prior or current dermatitis ($p=0.004$).

DISCUSSION

Recent data have demonstrated that non-atopic hemodialysis patients, despite continued exposure, are not at risk of developing latex allergy (6). Moreover, allergic contact dermatitis due to substances used in manufacturing hemodialysis devices is rarely reported (7). However, we observed a positive patch test in 16 patients (19.3%), and 9 reactions were considered clinically relevant. Most of the sensitizations were towards allergens normally employed in the European standard patch-test series. Therefore, contact allergy can be a relevant clinical problem in hemodialysis patients.

The exposure to rubber products can vary according to method of dialysis. Furthermore, the allergenicity can vary from one product to another based on the allergen content (7, 8).

The data on the frequency of latex sensitization in the general population are limited. Some authors have demonstrated that latex-specific IgE in 1000 volunteer blood donors was found among 6.5% of subjects (9). Therefore the prevalence of latex allergy among our hemodialysis patients appears to be lower than in the population generally. Many studies have demonstrated that initiation of hemodialysis leads to a significant improvement of *in vitro* T-cell activation, proliferation and release of pro-inflammatory cytokines (10, 11). In particular, the inhibition of T-cells to produce Th2 cytokines and the B lymphopenia observed in uraemic and hemodialysed patients (12) could explain the limited specific-IgE production

Table I. *Comparison of patch test (PT) responses*

	Patients with positive PT ($n=16$)	Patients with negative PT ($n=67$)	Statistical significance
Age (years)	52±12	53±12	$p=0.74$
Sex			
Males	9 (56%)	32 (48%)	$p=0.54$
Females	7 (44%)	35 (52%)	
Time on haemodialysis (months)	45±29	52±32	$p=0.41$
History of atopy	3 (19%)	3 (5%)	$p=0.08$
Pruritus	9 (56%)	26 (39%)	$p=0.16$
History of dermatitis	9 (56%)	13 (19%)	$p=0.004$

detected. The high level of total serum IgE that we observed in some patients does not seem to be a risk factor for latex allergy. Furthermore, a previous study has demonstrated a reduced frequency of type I hypersensitivity reactions in hemodialysed patients (13).

Although allergic-type reactions in these patients are frequently reported in the literature (1, 2, 14), mechanisms other than type-I hypersensitivity could be involved. In fact, patients with chronic renal failure have a high *in vitro* spontaneous histamine release and an abnormal complement activation. One can therefore hypothesize that certain severe hypersensitivity reactions during hemodialysis are not IgE-mediated (15).

Nevertheless, exposure to rubber chemicals can induce delayed reactions. In a previous study we demonstrated that type-I and type-IV hypersensitivity are independent (4) as confirmed here. In conclusion, our data indicate a low prevalence of latex allergy in patients undergoing chronic hemodialysis, and hemodialysis patients do not represent a risk group for latex allergy.

REFERENCES

1. Kraske GK, Shinaberger JH, Klaustermeyer WB. Severe hypersensitivity reaction during hemodialysis. Ann Allergy Asthma Immunol 1997; 78: 217–220.
2. Bousquet J, Maurice F, Rivory JP, Skassa-Brociek W, Florence P, Chouzenoux R, et al. Allergy in long-term hemodialysis. J Allergy Clin Immunol 1988; 81: 605–610.
3. Turjanmaa K, Reunala T, Rasanen L. Comparison of diagnostic methods in latex surgical glove contact urticaria. Contact Dermatitis 1988; 19: 241–247.
4. Nettis E, Dambra P, Soccio AL, Loria MP, Ferrannini A, Tursi A. Type I allergy to natural rubber latex and Type IV allergy to rubber chemicals in children with risk factors. Contact Dermatitis 2001; 44: 181–182.
5. Kalpaklioglu AF, Aydin G. Renal failure – a new risk group for latex allergy? Allergy 1999; 54: 406–407.
6. Gonzalo MA, Revenga F, Caravaca F, Pizarro JL. Epidemiologic study of contact dermatitis in hemodialysis patients. Invest Allergol Clin Immunol 1997; 7: 20–23.
7. Yunginger JW, Jones RT, Fransway, Kelso JM, Warner MA, Hunt LW. Extractable latex allergens and proteins in disposable medical gloves and other rubber products. J Allergy Clin Immunol 1994; 93: 836–843.
8. Penneys NS, Edwards LS, Katsikas JL. Allergic contact sensitivity to thiuram compounds in a hemodialysis unit. Arch Dermatol 1976; 112: 811–813.
9. Ownby DR, Ownby HE, McCullough JA, Shafer AW. The prevalence of anti-latex IgE antibodies in 100 volunteer blood donors. J Allergy Clin Immunol 1996; 97: 1188.
10. Kelly CJ. T cell function in chronic renal failure and dialysis. Blood Purif 1994; 12: 36–41.
11. Kaul H, Girndt M, Sester U, Sester M, Kohler H. Initiation of hemodialysis treatment leads to improvement of T-cell activation in patients with end-stage renal disease. Am J Kidney Dis 2000; 35: 611–616.
12. Zamauskaite A, Perez-Cruz I, Yaqoob MM, Madrigal JA, Cohen SB. Effect of renal dialysis therapy modality on T cell cytokine production. Nephrol Dial Transplant 1999; 14: 49–55.
13. De Filippi C, Piazza V, Efficace E, Galli F, Pisati P, Aprile C, et al. Dialysis hypersensitivity: a fading problem? Blood Purif 1998; 16: 66–71.
14. Bousquet J, Rivory J-P, Maurice F, Skassa-Brociek W, Larrson P, Johansson SG, et al. Allergy in chronic hemodialysis. 1. Double blind intravenous challenge with formaldehyde. Clin Allergy 1987; 17: 499–506.
15. Salem M, Ivanovich PT, Ing TS, Daugridas JT. Adverse effects of dialyzers manifesting during the dialysis session. Nephrol Dial Transplant 1994; 9 S2: 127–137.