

ORIGINAL ARTICLE

Prevalence and relevance of the positivity of skin prick testing in patients with chronic urticaria

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ABSTRACT

Many patients with chronic urticaria (CU) worry that foods or other allergens are responsible for their urticaria. Skin prick testing (SPT) may be one of the investigations used to provide a clear illustration. The purpose of our study was to assess the prevalence of positivity of SPT to food allergens and aeroallergens and their relevance in patients with CU, in order to demonstrate the diagnostic value of SPT in CU. We retrospectively reviewed case record forms of patients with chronic ordinary urticaria who underwent SPT in the Urticaria Clinic, Siriraj Hospital, during the period 2000–2004. The studied allergens included 16 food allergens and 12 aeroallergens. Eighty-eight patients were enrolled. The prevalence of positive SPT among patients with CU was 47.7%. Patients who had personal histories of atopy had statistically significant positive SPT results compared with patients who had negative SPT. Of 88 patients, 26 patients (30%) gave positive results to food allergens, 36 patients (41%) gave positive results to aeroallergens and 20 patients (22.7%) gave positive results to both food and aeroallergens. One-third of the subjects (34.6%) who had positive SPT results to food allergens had clinical relevance of food allergy in some systems but only one patient had clinical relevance of food-induced urticaria. Half of the patients who had a history of aeroallergen sensitivity gave a positive SPT response for aeroallergens; however, there was no clinical relevance to their CU. Our study showed that the prevalence of positive SPT to food allergens and aeroallergens in patients with CU was common but had little clinical relevance to CU.

Key words: prevalence, skin prick testing, urticaria.

INTRODUCTION

Episodes of acute urticaria/angioedema in some individuals with a personal or family history of asthma, rhinitis or eczema are presumed to be immunoglobulin (Ig)E-dependent, which urticaria/angioedema may accompany an exacerbation of asthma or rhinitis. However, the prevalence of chronic urticaria/angioedema is not increased in atopic individuals.¹

Food allergy is a recognized cause of acute urticaria, but the role of food components in chronic urticaria (CU) is controversial. The concept of food additives as a cause of CU was popularized in the European published work of the 1970s and 1980s. These studies involved challenge testing but some

studies were not placebo-controlled, and the reproducibility was not investigated.^{2–4}

In contrast, Mathews reported that food allergy was rarely a cause for CU and angioedema.⁵ Greaves also agreed with this concept. His routine use of placebo-controlled single-blind challenge testing for food additive intolerance, over a period of 20 years, indicates that patients who can reproducibly be shown to react to a food additive are extremely rare. The association between food and CU mostly resulted from non-allergic reaction or pseudoallergic reaction to food preservatives and dyes, accounting for just 5% of chronic idiopathic urticaria.⁶

Skin prick testing (SPT) can provide useful confirmatory evidence for immediate hypersensitivity

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(type I allergy). It demonstrates tissue-bound IgE and identifies the atopic state. However, a positive SPT merely identifies sensitization to a particular allergen, it does not predict clinical relevance independent of the history.

Skin prick testing has some roles in patients with acute urticaria and angioedema who have histories of food allergy and/or histories of exacerbation of urticaria accompanied by exacerbation of allergic rhinitis and/or asthma.⁷ Yocum *et al.* reported that 123 of 179 patients (69%) with histories of acute urticaria and anaphylaxis had positive SPT results.⁸

Many patients with chronic ordinary urticaria attribute exacerbations of their urticaria to what they have eaten, even though these reactions are very rarely immediate, and commonly are not reproducible. Some patients worry that foods or other allergens were responsible for their urticaria even though it had been thoroughly explained by doctors. SPT may be one of the investigations to provide a clear illustration for patients which may reinforce verbal advice. Quaranta *et al.* studied SPT in 22 of 86 patients with CU and 13 patients (59%) gave positive SPT results.⁹

The purpose of our study was to assess the prevalence of positivity of SPT to food allergens and aeroallergens and their relevance in patients with CU, in order to demonstrate the diagnostic value of SPT in CU.

METHODS

This study was approved by the ethical committee on research involving human subjects of Siriraj Hospital. We retrospectively reviewed case record forms of patients with chronic ordinary urticaria who underwent SPT at the Urticaria Clinic, Siriraj Hospital, during the period 2000–2004.

Chronic urticaria is defined as any pattern of recurrent urticaria occurring at least twice a week for at least 6 weeks.¹⁰ Etiology of CU was evaluated by a complete history of possible causes, physical examination and laboratory tests. Patients who had obvious identified etiological factors (i.e. physical urticaria, drug-induced urticaria, systemic lupus erythematosus and urticarial vasculitis) were excluded from the study. Besides SPT, other laboratory investigation included complete blood counts, urinalysis,

erythrocyte sedimentary rate, stool examination and other investigations that were necessary for the individuals; these were blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, bilirubins, total protein, albumin, hepatitis B virus surface antigen, anti-hepatitis C virus, free T3, free T4, thyroid stimulating hormone, antithyroid autoantibodies (i.e. antithyroglobulin and antimicrosomal antibodies) antinuclear antibodies, cryoglobulins, serum complement level, chest and sinus X-ray studies.

All consecutive patients aged older than 18 years were included. All subjects were informed about the course of SPT and gave signed consent prior to the beginning of the test. The following data were collected: demographic data for age, sex, history of food allergy, personal and family history of atopy and the history of aeroallergen-induced urticaria.

Patients were not tested if they had taken short-acting antihistamines within the preceding 3 days or long-acting antihistamine drugs within the preceding 7 days or systemic corticosteroids equivalent to more than 10 mg of prednisolone per day within the preceding 28 days before skin testing. The application of high potency, topical corticosteroids to the tested area was avoided for 3 weeks prior to testing.¹¹

Skin prick testing

The SPT is performed by placing a drop of antigen extract on the skin then using a hypodermic needle to gently tent the skin and puncture it in order to introduce the allergen and 0.9% saline and 10 mg/mL histamine were included as negative and positive controls, respectively. In all patients, skin reactivity was tested on the volar surface of the forearm by the same trained and experienced person. The results were read at 15 min. A positive result yields a wheal at least 3 mm in diameter larger than the negative control.¹² The studied allergens (Alk-Abello; Lincoln Diagnostics, Dallas, TX, USA), included 16 food allergens (egg white, egg yolk, cow milk, wheat, banana prawn, giant tiger prawn, giant freshwater prawn, undulated surf clam, green mussel, blue swimming crab, sea crab, snapper, cuttlefish, butterfly, mackerel and yeast) and 12 aeroallergens composed of molds (*Aspergillus*, *Penicillium*, *Cladosporium*), pollens (paragrass, bermuda grass, careless weed), house dust, mites (*Dermatophagoides pteronyssinus*,

Table 1. Demographic data of patients studied

	Total (<i>n</i> = 88)	SPT positive (%) (<i>n</i> = 42)	SPT negative (%) (<i>n</i> = 46)	<i>P</i> -value
Age, mean (SE)	37 (1.2)	36 (1.8)	38 (1.7)	0.5
Sex, <i>n</i> (%)				
- female	76 (86.4)	34 (44.7)	42 (55.3)	0.1
History of food allergy, <i>n</i> (%)	50 (56.8)	24 (48.0)	26 (52.0)	0.9
Personal history of atopy, <i>n</i> (%)*	28 (31.8)	20 (47.6)	8 (17.4)	0.002
- AR	18	12	6	0.071
- Asthma	6	5	1	0.070
- AD	1	1	0	0.3
- AC	3	2	1	0.5
Family history of atopy, <i>n</i> (%)	29 (33%)	17 (58.6)	12 (41.1)	0.1
- AR	21	11	10	0.6
- Asthma	7	5	2	0.2
- AD	0	0	0	
- AC	0	0	0	
History of aeroallergen-induced urticaria, † <i>n</i> (%)	13 (14.8)	7 (53.8)	6 (46.2)	0.6

AD, atopic dermatitis; AC, allergic conjunctivitis; AR, allergic rhinitis; SPT, skin prick test. **P* < 0.05. †Urticarial wheals were frequently accompanied by an exacerbation of asthma or allergic rhinitis.

Table 2. Skin prick test results in patients with various histories

History	No. of cases	SPT positive, <i>n</i> (%)	No. of cases							SPT negative, <i>n</i> (%)
			Food allergen positive	R1	Aeroallergen positive	R1	R2	Food + aeroallergen positive	R1	
Personal history of atopy*	28	20 (71.4)	14	0	17	0	17	11	0	8 (28.6)
History of food reaction	50	24 (48)	13	1	20	0	0	9	0	26 (52)
History of aeroallergen-induced urticaria	13	7 (53.8)	2	0	6	0	5	1	0	6 (46.2)
Family history of atopy	29	17 (58.6)	11	0	15	0	15	9	0	12 (41.4)

SPT, skin prick test; R1, relevance to urticaria; R2, relevance to their atopic state; **P* < 0.05.

Dermatophagoides farinae), cat hair, dog epithelium and cockroach.

Statistical analysis

Descriptive statistics, such as mean, median, minimum, maximum and percentages, were used to describe demographic data and positivity of SPT, and χ^2 -test was used for the statistical analytical approach. All statistical data analyses were performed using SPSS for Windows ver. 10.0 (SPSS Software, Chicago, IL, USA).

RESULTS

Eighty-eight patients were enrolled, of whom 12 were male (13.6%) and 76 female (86.4%). Their mean age was 37.1 years with a range of 18–65 years.

Table 1 shows the demographic data of the patients studied. Two-thirds (56.8%) of them gave a history of food allergy. Personal and family history of atopy were reported in 31.8% and 33%, respectively. The commonly associated atopic conditions were mainly allergic rhinitis and asthma. Personal history of aeroallergen-induced urticaria was found in 14.8%.

Of the 88 patients tested, 42 (47.7%) had a positive reaction to at least one allergen. Among these 42 patients, 26 (63.4%) had positive SPT results to food allergens, and 36 patients (85.7%) had positive results to aeroallergens. Twenty patients (47.6%) had positive results to both food allergens and aeroallergens (data not shown in the table).

Table 2 shows the details of SPT results. Patients who had personal histories of atopy had statistically significant positive SPT results compared with patients

Table 3. Details of patients who had positive skin prick tests (SPT) to food ($n = 26$)

Characteristic	n (%)
SPT positive to aeroallergens	20 (76.9)
Personal history of atopy	14 (53.8)
History of food reaction	13 (50)
Family history of atopy	11 (42.3)
Relevance of SPT to clinical food allergy	9 (34.6)
History of aeroallergen induced urticaria	2 (7.7)
Clinical of food induced urticaria	1 (3.8)

who had negative SPT (71.4% vs 28.6%, $P < 0.05$). Concerning the patients who gave positive histories of reaction to food (e.g. such as claiming that seafood was the cause of their urticarial wheals), approximately half of them (48%) had positive results to SPT. However, when careful histories were taken, only four out of 50 patients (8%) had reliable histories of food-induced urticaria and there was only one out of 50 patients who gave a positive reaction to SPT. Family history of atopy and history of aeroallergen-induced urticaria produced no statistical significance on the result of SPT to food. Half of the patients who had histories of aeroallergen sensitivity gave positive SPT responses for aeroallergens; however, there was no clinical relevance to their urticaria.

Table 3 shows the details of the patients regarding positive SPT results to food allergens. Of 26 patients who gave a positive result to food allergens, approximately half of them (50% and 53.8%) had a history of food reaction and a personal history of atopy, respectively, while 11 of them (42.3%) had a positive family history of atopy. One-third of the subjects (34.6%) who had a positive SPT result to food allergens

had clinical relevance of food allergy in some systems such as gastrointestinal disorders, asthma and migraine but only one patient had clinical relevance of food-induced urticaria. Coexisting positive SPT to food and aeroallergen was found in 20 of 26 patients (77%).

Table 4 shows various studies concerning the prevalence of positive SPT results in patients with CU, ranging 26–64%. In our study, the prevalence of positive SPT among patients with CU was 47.7%. Of 88 patients, 26 patients (30%) gave positive results to food allergens (one to egg white, one to cow milk, two to wheat, eight to banana prawn, 11 to giant tiger prawn, five to giant freshwater prawn, five to green mussel, 11 to blue swimming crab, eight to sea crab, two to snapper, three to cuttlefish, four to butterfish and three to mackerel), 36 patients (41%) gave positive results to aeroallergens (one to *Aspergillus*, two to *Penicillium*, one to *Cladosporium*, nine to para grass, 14 to bermuda grass, 12 to careless weed, 17 to house dust, 34 to mites, four to cat hair and 12 to dog epithelium), 20 patients (22.7%) gave positive results to both food and aeroallergens.

DISCUSSION

Many allergens, such as house dust mites, animal dander, pollens, molds or even variable foods, are present in the environment and disturb our lifestyle.¹³ Ingestion of foods, commonly fish, shrimps, nuts, eggs and milk, may elicit allergic symptoms such as angioedema, asthma, urticaria or systemic anaphylactic reaction. It was generally accepted that different dietary habits between Asian and Western countries

Table 4. Various studies concerning the prevalence of positive skin prick test (SPT) in patients with chronic urticaria

Authors	Types	Allergens	Positive SPT	
			n (total)	%
Mahesh <i>et al.</i> ¹⁷	CU	Aeroallergens	78 (122)	64
Quaranta <i>et al.</i> ⁹	CU	N/A	13 (22)	59
Liutu <i>et al.</i> ¹⁸	CU	Food and aeroallergens	47 (91)	51
Caliskaner <i>et al.</i> ¹¹	CU	Aeroallergens	71 (259)	27.4
Malanin <i>et al.</i> ¹⁹	CU	Food	24 (91)	26
Our study	CU	Food	26 (88)	30
		Aeroallergens	36 (88)	41
		Food + aeroallergens	20 (88)	22.7
		≥ 1 allergen	42 (88)	47.7

CU, chronic urticaria; N/A, not available.

as well as socioeconomic status may be relevant in causing sensitization.¹⁴

The SPT is used to identify specific IgE sensitization. It has some roles in patients with acute urticaria and angioedema who have histories of food allergy and/or histories of exacerbation of urticaria accompanied by exacerbation of allergic rhinitis and/or asthma. Nevertheless, SPT can provide useful confirmatory evidence for a diagnosis made on clinical grounds. A positive test merely identifies sensitization to a particular allergen, it does not predict clinical relevance independent of the history.¹⁵

Many cases of ordinary urticaria, previously regarded as idiopathic, can now be ascribed to autoimmunity. It was demonstrated that anti-FcεRI-positive serum from patients with CU was able to induce histamine release from basophils.¹⁰ The reported prevalence of positive SPT in patients with CU ranged 26–64% (Table 4).

Mahesh *et al.* reported their SPT study in patients with CU, and 78 out of 122 (64%) patients had skin sensitivity to antigen of house dust mites (*D. pteronyssinus* and *D. farinae*).¹⁶ Quaranta *et al.* reported that 13 out of 22 (59%) patients with CU had positive SPT results. However, they did not mention the types of allergens they used.⁹ Liutu *et al.* reported that 47 out of 91 (51%) patients with CU had positive SPT results to food and aeroallergens: 26 reacted to food (10 to cereal, eight to shrimp and fish, four to spices and seven to various compounds including vegetables, fruits, nuts, meat, milk and egg), 14 to pollens, 11 to animal epithelium, nine to mites, five to mold and yeast.¹⁷ Caliskaner *et al.* investigated SPT reactivity to aeroallergens (mites, pollens, molds, animal danders and cockroaches) in patients with CU but without allergic rhinitis and/or asthma, and 71 patients out of 259 (27.4%) gave positive results.¹¹ Moreover, Malanin *et al.* performed SPT using food additives in patients suffering from CU, and 24 out of 91 (26%) patients had a positive skin test response.¹⁸ Our study demonstrated a prevalence of positive SPT to food allergens of 30% and to aeroallergens of 41%, and 22.7% to both food and aeroallergens. However, only one case out of 88 cases (1.1%) with CU who underwent SPT had clinical relevance to food allergens. When careful reviewing of this patient's history was performed, it was discovered that she lived near the sea and she usually ate crab without

knowing that she had a seafood allergy which exacerbated her urticaria. After that, an oral food challenge was done and it was revealed that she was definitely allergic to seafood.

A negative SPT response has excellent negative predictive value for excluding the presence of IgE-mediated reaction but the positive skin test in isolation cannot be considered proof of a clinically relevant food allergy. A positive SPT indicates only food sensitizations; that is, the presence of food-specific IgE antibodies.^{19,20} An adverse food reaction is not only from allergic reaction to the food antigens but also from non IgE-mediated reaction to food additives such as flavorings, coloring and preservatives. An oral food challenge is the best method to diagnose food intolerance.^{20–22}

Supakthanasiri *et al.* reported that the prevalence of positive SPT to at least one out of 16 common aeroallergens in 100 healthy Thai adults was 42%.²³ This percentage was comparable with our study performed on CU patients of whom 36 patients (41%) gave positive results to aeroallergens. In 2001, Vichyanond *et al.* reported that the prevalence of allergic rhinitis and asthma in Thai university students was 26.3% and 8.8%, respectively.²⁴ Kulthanan *et al.* reported that the prevalence of allergic rhinitis and asthma in 450 Thai CU patients was 20% and 4.4%, respectively.²⁵ The data implied that the prevalence of atopy was not increased in patients with CU. Concerning patients with atopic diseases, Kulthanan *et al.* had also performed SPT with 13 common aeroallergens in Thai patients with adult atopic dermatitis and showed positive results in 19 of 29 patients (65.5%) (unpubl. data). Because the prevalence of positive SPT is much influenced by the proportion of subjects having atopic diseases, the mentioned data implies that there is no increased prevalence of positive SPT to aeroallergens between patients with CU and the normal healthy population.

In summary, our study showed that the prevalence of positive SPT to food allergens and aeroallergens in patients with CU was common but had little clinical relevance to CU.

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