

Prevalence of food avoidance and food allergy in Chinese patients with chronic urticaria

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Summary

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Accepted for publication

6 November 2011

Funding sources

None.

Conflicts of interest

None declared.

DOI 10.1111/j.1365-2133.2011.10733.x

Background Food avoidance is common among Chinese patients with chronic urticaria because food allergy is considered to be the cause of disease. The benefit of food avoidance and its relationship with food allergy is unknown.

Objectives The aims of this study were to examine the prevalence and effect of food avoidance and food allergy in patients with chronic urticaria.

Methods Four hundred and ninety-four patients with chronic urticaria, who attended Peking University Third Hospital from January 2009 to December 2010, were studied. Food avoidance and its effect were investigated with a detailed questionnaire. Food allergy was diagnosed by serum food-specific immunoglobulin E (IgE), elimination diet based on food-specific IgE, and open food challenge.

Results One hundred and fifty-eight patients (32%) avoided fish, shrimp, crab, lamb or beef prior to evaluation and 82.9% of them reported food avoidance ineffective. Out of 341 patients tested for serum food-specific IgE, 75 (22%) were positive, with soy, peanut, beef, lamb, chicken, crab and shrimp as the leading allergens. Chronic urticaria induced by food allergy was found in only 2.8% of patients.

Conclusions The prevalence of food avoidance is high and mostly ineffective in Chinese patients with chronic urticaria. Foods avoided do not correspond to serum food-specific IgE. The incidence of IgE-mediated urticaria, as demonstrated by open food challenge, is low. Physicians and patients should be aware of unnecessary dietary avoidance while seeking treatment of chronic urticaria.

Chronic urticaria is defined as spontaneous urticaria that persists for longer than 6 weeks. It is a heterogeneous disease in which allergy may be involved.¹ However, food allergy is a rare cause of the disease.¹

A food allergy is defined as an adverse health effect arising from a specific immune response, which occurs reproducibly on exposure to a given food.² Specific immunoglobulin E (sIgE)-mediated food allergies are immediate, reproducible and readily diagnosed by detection of food-sIgE.³ Urticaria is one of the symptoms of food-induced allergic reactions but IgE-mediated food allergy is rarely the underlying cause of chronic spontaneous urticaria.⁴⁻⁶

In China, food allergy is often accredited as the cause of urticaria; therefore, food avoidance becomes common among patients. The foods considered allergenic by Chinese patients with chronic urticaria include fish, shellfish, beef, lamb, egg and spicy foods. Patients choose or rather are told by physicians to eliminate these foods from their diet without further diagnostic procedures. However, whether or

not these foods actually induce chronic urticaria is unknown.

The prevalence of food avoidance and its effect on the prognosis of chronic urticaria has not been evaluated. Furthermore, avoiding particular foods restricts the patient's lifestyle, and may ultimately be harmful to the patient's health and wellbeing. The aim of this study was to assess the prevalence and effect of food avoidance in patients with chronic urticaria, and its relationship with food allergy.

Materials and methods

Patients

Four hundred and ninety-four Chinese Han patients with chronic spontaneous urticaria, who attended Peking University Third Hospital Dermatology Department from January 2009 to December 2010, were enrolled in the study. There were 183 men (37%) and 311 women (63%). The average age was

38.6 ± 17.7 years (range 2–82); median duration of disease was 6 months [interquartile range (IQR) 21]. No history of anaphylaxis was found. The local ethics committee approved this study and oral consent was given by all participants.

Investigation of food avoidance

The prevalence and effect of food avoidance were obtained by questionnaire completed by each participant, to include a careful history of urticaria symptoms, and past medical and allergy history. Each patient presented details of his or her eating habits and foods avoided prior to evaluation.

Detection of serum food-specific immunoglobulin E

Serum samples from 341 patients who consented to sIgE detection were analysed for food allergen-sIgE antibodies using the IVT Allergy Screen™ (Arlington Scientific, Inc., Springville, UT, U.S.A.), following the procedure described in the packet insert. Serum food-sIgE antibodies detected included soy, peanut, beef, lamb, chicken, crab, shrimp, fish, egg, milk, scallop and salmon. Skin prick test was not chosen in this study because the process can be uncomfortable for some patients and interpretation of results is time consuming.

Elimination diet based on serum food-specific immunoglobulin E

After detection of serum food-sIgE, an elimination diet was administered by eliminating food items based on food-sIgE from the diet for 2 weeks. Patients were educated to eliminate specific foods and, through the reading of food labels, to avoid accidentally ingesting food allergens. If there was no improvement with elimination, then the foods eliminated were not likely to be a cause of the complaints and reintroduction into the diet was advised.

Oral food challenge

Food challenge ultimately confirms or disproves specific foods as the cause of clinical disease.⁷ If food challenge elicits no symptoms, then food allergy can be ruled out; but when food challenge elicits objective symptoms correlating with the patient's medical history and supported by laboratory tests, then a diagnosis of food allergy is supported.² The double-blind placebo-controlled food challenge (DBPCFC) is the standard method by which food allergy is determined. However, the development of recipes and preparation of masked foods is time consuming, which makes DBPCFC with masked foods difficult to perform in clinical practice. Therefore, open food challenge was chosen in this study. Open food challenge included reintroduction of foods that patients had avoided prior to evaluation and of foods eliminated based on food-sIgE during the elimination diet. This test was performed in patients with both food avoidance without corresponding serum food-sIgE, and with serum food-sIgE.

Statistical analysis

Data were analysed by conducting Student's t-test, Mann–Whitney U-test, and χ^2 test, using SPSS 18.0 (SPSS Inc., Chicago, IL, U.S.A.). Results were considered significant at a P-value < 0.05.

Results

Out of 494 patients with chronic urticaria, 158 patients (32%) avoided suspicious foods prior to evaluation. There were 50 men (31.6%) and 108 women (68.4%); average age was 40.2 ± 18.9 years (range 2–81); median duration of disease was 6 months (IQR 21). Of the 336 patients (68%) who had a normal diet, 133 were men (39.6%) and 203 were women (60.4%); average age was 37.8 ± 17 years (range 2–82); median duration of disease was 6 months (IQR 21). Age was not significantly different between the food avoidance group and the normal diet group (40.2 ± 18.9 years vs. 37.8 ± 17 years, $P > 0.05$, Student's t-test), neither was gender (50 men and 108 women vs. 133 men and 203 women, $P > 0.05$, χ^2 test), nor the duration of disease [6 (3–24) months vs. 6 (3–24) months; $z = -1.314$, $P > 0.05$, Mann–Whitney U-test].

The prevalence and effect of food avoidance

One hundred and fifty-eight (32%) out of 494 patients with chronic urticaria avoided suspicious foods prior to evaluation. Twenty-seven patients (17.1%) claimed their symptoms improved after food avoidance, but did not achieve complete remission; 131 patients (82.9%) reported food avoidance ineffective. Table 1 shows the prevalence of leading foods avoided and the effect.

Serum food-specific immunoglobulin E

Three hundred and forty-one patients were tested for serum food-sIgE. There were 130 men (38%), 211 women (62%) with an average age of 38.9 ± 17.6 years (range 2–82); median

Table 1 Prevalence and effect of food avoidance in 494 patients studied

Food avoided	No. of patients avoiding foods before evaluation (%)	No. of patients claiming food avoidance ineffective (%)
Fish	94 (19)	84 (89.4)
Shrimp	91 (18.4)	84 (92.3)
Crab	82 (16.6)	80 (97.6)
Spicy food	72 (14.6)	58 (80.1)
Lamb	42 (8.5)	39 (92.9)
Beef	36 (7.3)	34 (94.4)
Egg	15 (3)	14 (93.3)
Milk	12 (2.4)	9 (75)

Table 2 Prevalence of serum food-specific immunoglobulin E to each food allergen in 341 patients tested

Specific IgE	No. of positive (%)
Soy and peanut	35 (10.3)
Beef, lamb and chicken	16 (4.7)
Crab and shrimp	13 (3.8)
Fish	11 (3.2)
Egg	10 (2.9)
Cow's milk	5 (1.5)
Scallop and salmon	3 (0.9)

duration of disease was 6 months (IQR 21). Seventy-five patients (22%) had positive serum food-sIgE (Table 2).

Out of 341 patients who were tested for serum food-sIgE, 108 patients (32%) had avoided suspicious foods prior to evaluation. There were 30 men (28%) and 78 women (72%), with an average age of 41.9 ± 17.9 years, (range 7–81); median duration of disease was 6 months (IQR 21). Seventeen patients (16%) had positive serum food-sIgE. The foods avoided prior to evaluation were not consistent with serum food-sIgE (Table 3).

Out of 341 patients who were tested for serum food-sIgE, 233 patients (68%) had a normal diet. There were 100 men (43%), 133 women (57%), with an average age of 37.5 ± 17.3 years (range 2–82); median duration of disease was 7 months (IQR 20). Fifty-eight patients (25%) had positive serum food-sIgE, which was not significantly different compared with the food avoidance group (25% vs. 16%, $P > 0.05$, Student's *t*-test).

Elimination diet and open food challenge based on serum food-specific immunoglobulin E

Out of the 75 patients who tested positive for serum food-sIgE, 59 patients (89%) implemented an elimination diet for 2 weeks. Seven patients (11%) refused an elimination diet: five of these patients claimed to have achieved complete remission, suggesting that food allergy could be ruled out; two patients still had symptoms (whether or not they are allergic to foods detected by serum food-sIgE remains unclear). Eight patients and one deceased patient were lost to follow-up, making diagnosis of food allergy based on an elimination diet unknown in a total of 11 patients. Of the 59 patients who implemented an elimination diet, 73% of them claimed to have fully recovered after eliminating foods based on serum food-sIgE. Fifty-one (86%) of the 59 patients who implemented an elimination diet performed an open food challenge; eight patients (14%) refused. Thus, a total of 19 patients could not be evaluated for food allergy. In the remaining 322 patients who tested for serum food-sIgE, nine patients experienced weals and itching after ingesting sIgE foods. Therefore, the prevalence of food-induced urticaria was 2.8% (nine out of 322).

Two hundred and sixty-six (78%) patients tested negative for serum food-sIgE and 71% claimed to have achieved remission,

which was not significantly different from patients with positive serum food-sIgE (71% vs. 73%, $P > 0.05$, χ^2 test).

Six out of 266 patients with negative food-sIgE claimed to have urticarial symptoms after ingesting the foods they had avoided. These patients can be categorized as having food pseudoallergy.

Discussion

Food allergy is often incriminated as the cause of chronic urticaria because of the difficulties in identifying the intrinsic cause of the disease. As a result, patients avoid certain foods based on self-perceived food allergy, or are advised by physicians to avoid certain foods without further investigation. In this study, prevalence of food avoidance was high (32%) among Chinese patients with chronic urticaria; this result was similar to those in previous publications by Juhlin⁴ and Sayag *et al.*,⁸ where 30–40% of patients with chronic urticaria attributed their symptoms to food intolerance, and 20% of adults and children altered their diets for perceived adverse reactions or allergies.⁹ In the United States, 25% of the population believe they have allergic reactions to foods,^{3,9,10} and 9% of American adults self-reported having a food allergy.¹¹

In the 158 patients who carried out food avoidance, the foods most commonly suspected of causing food allergy were fish, shrimp and crab (60%, 58% and 52%, respectively). These results were similar to the foods most commonly incriminated in Norway and Spain,¹² but different from those in a study by Eriksson *et al.*,¹³ where citrus fruits, chocolate, apple, hazelnut, strawberry, fish, tomato, egg and milk were suspected by patients in Russia, Estonia and Lithuania; and tree nuts, apple, pear, kiwi, stone fruits and carrot were considered as allergens in Sweden and Denmark. Also, foods considered responsible for food allergy in American adults were peanuts, tree nuts, egg, milk, wheat, soybeans, fish and shellfish.¹¹

In this study, food avoidance was found ineffective in 83% of patients, indicating that dietary restriction based on the assumption of food allergy was unnecessary and would not lead to clinical remission.

A therapeutic approach in chronic urticaria is the identification and elimination of the underlying causes and/or eliciting triggers.¹ A study done by Kaeser *et al.*¹⁴ proposed that chronic urticaria might be triggered by food allergy; Hamilton and Franklin Adkinson¹⁵ suggested serum immunoassay to determine food-sIgE antibodies could provide a modality to evaluate IgE-mediated food allergy. In this study, serum food-sIgE for one or more foods was found in 75 patients (22%) with chronic urticaria, similar to the proportion reported by Kaeser *et al.*,¹⁴ which was 27%.

The most common food allergens detected in this study were soy and peanut (10%), beef, lamb and chicken (5%), and crab and shrimp (4%) (Table 2). These results were inconsistent with the foods avoided prior to evaluation (Tables 1 and 3), but similar to commonly reported allergens worldwide.³

Table 3 Food avoidance, elimination diet and open food challenge in 17 patients with positive food-specific immunoglobulin E (food-sIgE)

Case no.	Sex/age (years)	Duration of food avoidance (months)	Food(s) avoided before evaluation	Serum food-sIgE	Food(s) eliminated based on sIgE	Open food challenge	Clinical Recovery	Food(s) avoided after evaluation
1 ^a	F/53	2	Fish Shrimp Crab Spicy foods	Crab Shrimp	Crab Shrimp	Fish ⁻ Shrimp ⁺ Crab ⁺ Spicy foods ⁺	Yes	Shrimp Crab Spicy foods
2	F/49	> 24	Shrimp Crab Beef Lamb	Fish	Fish	Shrimp ND Crab ND Beef ⁻ Lamb ⁻ Fish ND	Yes	Fish Shrimp Crab
3	M/64	12	Fish Shrimp Crab Spicy foods	Fish Crab Soy Peanut	Deceased	Deceased	-	-
4	F/21	> 24	Milk	Cow's milk	Cow's milk	Cow's milk ⁻	No	None
5	M/36	> 24	Beef Lamb	Crab Shrimp	Crab Shrimp	Beef ⁻ Lamb ⁻ Crab ⁻ Shrimp ⁻	Yes	None
6	F/32	3	Shrimp	Fish	Fish	Shrimp ND Fish ND	Yes	Fish Shrimp
7	F/60	> 24	Fish Shrimp Crab Beef Lamb	Soy Peanut Scallop Salmon	Soy Peanut Scallop Salmon	Fish ND Shrimp ND Crab ND Soy ND Peanut ND Scallop ND	No	Fish Shrimp Crab Beef Lamb Soy Peanut Scallop
8	M/40	> 24	Spicy foods	Soy Peanut	Soy Peanut	Spicy foods ⁻ Soy ⁻ Peanut ⁻	Yes	None
9	M/81	> 24	Fish Shrimp Crab Spicy foods	Fish Beef Lamb Chicken	Fish Beef Lamb Chicken	Fish ND Shrimp ⁻ Crab ND Spicy foods ⁻ Beef ⁻ Lamb ⁻ Chicken ⁻	Yes	Fish Crab
10	F/28	2	Beef Lamb	Egg Crab Shrimp	Egg Crab Shrimp	Beef ⁻ Lamb ⁻ Egg ⁻ Crab ⁻ Shrimp ⁻	Yes	None
11	M/49	9	Egg	Crab Shrimp	Crab Shrimp	Egg ⁻ Crab ⁻ Shrimp ⁻	Yes	None
12	M/30	2	Fish Shrimp Crab	Fish Scallop Salmon	Fish Scallop	Fish ND Shrimp ND Crab ND Salmon ND Scallop ND	No	Fish Shrimp Crab Salmon Scallop
13 ^b	F/18	9	Beef Lamb	Soy Peanut	Soy Peanut	Beef ⁻ Lamb ⁻ Soy ⁻ Peanut ⁻	Yes	Beef Lamb

Table 3 (Continued)

Case no.	Sex/age (years)	Duration of food avoidance (months)	Food(s) avoided before evaluation	Serum food-sIgE	Food(s) eliminated based on sIgE	Open food challenge	Clinical Recovery	Food(s) avoided after evaluation
14	F/54	3	Fish Shrimp Crab Beef Lamb	Soy Peanut	Soy Peanut	Fish ND Shrimp ND Crab ND Beef ⁻ Lamb ⁻ Soy ⁻ Peanut ⁻	Yes	Fish Shrimp Crab
15	F/27	12	Fish	Soy Peanut	Soy Peanut	Fish ND Soy ⁻ Peanut ⁻	Yes	Fish
16	F/67	10	Fish Shrimp Crab Egg	Soy Peanut	Soy Peanut	Fish ND Shrimp ND Crab ND Egg ⁻ Soy ⁻ Peanut ⁻	No	Fish Shrimp Crab
17	F/35	2	Egg	Egg	Egg	Egg ⁻	Yes	None

^aFood allergy diagnosed by open food challenge. ^bContinued food avoidance after food allergy was disproved. ⁺Positive food challenge. ⁻Negative food challenge. NDFood challenge not done.

A favourable result of an elimination diet in patients with atopic dermatitis was reported by Agata *et al.*¹⁶ In this study, we examined the effect of elimination diets on patients with chronic urticaria. Complete remission was achieved by 73% of patients who implemented an elimination diet, suggesting that these patients may be allergic to the foods detected by serum sIgE. However, in patients with food-sIgE, 51 patients performed an open food challenge and nine of them were positive. A final diagnosis of food allergy was made in only 3% of patients; this was similar to other studies, where a high prevalence of food allergy was reported by patients but actual incidence confirmed by food challenges comprised < 2% of cases.³ These results suggest that food challenges are necessary for the diagnosis of food allergy; the outcome of an elimination diet alone is unreliable. In addition, because the remission rates of patients practising elimination diets and testing positive (73%) were observed to be strongly similar to those of patients testing negative (71%), food avoidance was believed not to be the sole contributor for remission.

Psychological factors must be taken into consideration in the assessment of food avoidance and food allergy. Patients' perception of food allergy led to food avoidance and, in some cases, patients continued to avoid these foods even after food allergy was disproved by scientifically validated tests. In this study, eight patients continued food avoidance and refused open food challenge due to the beliefs of food-induced urticaria. One patient continued food avoidance even after food-induced urticaria was contradicted by open food challenge (patient 13, Table 3).

The foods proven to induce urticaria by open food challenge in this study were cow's milk (two cases), egg (two

cases), crab and shrimp (two cases), fish (one case), soy and peanut (one case), beef, lamb and chicken (one case). This result was similar to those reported in the United States, where egg, milk, peanut, tree nuts, fish, shellfish, wheat and soy account for most significant food allergies.⁶

In 17 patients with food avoidance (Table 3), only one (patient 1) was diagnosed with food allergy by open food challenge, but the foods avoided did not correspond to serum food-sIgE. Patients were able to achieve remission after food avoidance was stopped, and no symptoms were elicited when the foods avoided prior to evaluation were reintroduced into the diet. This result indicated that food avoidance was unnecessary. When food allergy was not proved by the open food challenge, patients were able to reintroduce suspicious foods back into their diet.

Pseudoallergy can be considered in patients with negative diagnostic screening,¹⁷ and a pseudoallergen-free diet is the approach for identifying patients who will benefit from avoiding pseudoallergens. A study done by Zuberbier *et al.*⁵ reported improvement or cessation of urticarial symptoms in 73% patients who were tested on pseudoallergen-free diets. Moreover, Magerl *et al.*¹⁸ proposed that a pseudoallergen-free diet is beneficial for one in three patients. In this study, six patients displayed negative serum food-sIgE but claimed to have adverse reaction to certain foods; a pseudoallergen-free diet may be the next diagnostic approach for these patients to rule out pseudoallergy.

In conclusion, the prevalence of food avoidance was high and mostly ineffective in Chinese patients with chronic urticaria. Foods avoided did not correspond to serum food-sIgE. The incidence of food-induced urticaria, as demonstrated by

open food challenge, is low. Physicians and patients should be aware of unnecessary dietary avoidance while seeking treatment of chronic urticaria. Other types of food reactions such as pseudoallergy or food intolerance have been found to play a role in chronic urticaria and should be further studied.

What's already known about this topic?

- Immunoglobulin-E-mediated food allergy is rare in chronic urticaria.
- Food avoidance alone, without the demonstration of food allergy by food challenge, is unnecessary.
- Elimination diet alone is unreliable in identifying food allergy.

What does this study add?

- Food avoidance is common in Chinese patients with chronic urticaria. Patients choose, or are told by physicians to eliminate suspicious foods from their diet without further diagnostic procedures.
- Food avoidance is high among patients with chronic urticaria in China but found to be mostly ineffective in this study.
- Foods avoided were inconsistent with serum food-specific immunoglobulin E (IgE).
- Chronic urticaria induced by IgE-mediated food allergy is uncommon.

Acknowledgments

The authors express their thanks to the Department of Epidemiology of Peking University Third Hospital for their help with statistical analysis.

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