

Diagnostic Value of the Serum-Specific IgE Ratio of ω -5 Gliadin to Wheat in Adult Patients with Wheat-Induced Anaphylaxis

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Key Words

Anaphylaxis • Gliadin • Immunoglobulin E • Wheat hypersensitivity

Abstract

Background: Wheat is an important food allergen associated with severe allergic reactions, including wheat-dependent exercise-induced anaphylaxis (WDEIA) and wheat-induced anaphylaxis (WIA). To diagnose WDEIA, an exercise challenge test following wheat ingestion is performed, which is time-consuming and unsafe. The compound ω -5 gliadin has been identified as a major allergen for WDEIA and WIA. We evaluated the diagnostic value of serum immunoglobulin E (IgE) ratios of ω -5 gliadin to wheat in adult patients with WDEIA or WIA. **Methods:** In total, 27 patients were enrolled and classified into 2 groups according to the severity of their allergic reactions to wheat. Serum IgE, specific to wheat and ω -5 gliadin, was measured using the ImmunoCAP system. To evaluate the diagnostic value, receiver operator characteristic curves were produced. **Results:** Group 1 included 17 patients with a history of anaphylaxis and group 2 included 10 patients having urticaria or atopic dermatitis. Serum IgE specific to wheat was increased in 47% of group 1

and 100% of group 2. However, all patients in group 1 had high serum IgE specific to ω -5 gliadin, whereas only 20% of group 2 showed increased levels. To identify a better diagnostic value, the log-transformed IgE ratio of ω -5 gliadin to wheat was calculated, with the cutoff value at 0.3. Based on these criteria, we found 100% sensitivity and specificity. **Conclusions:** This study confirms that the serum IgE ratio of ω -5 gliadin to wheat may be a useful marker for the diagnosis of WDEIA and WIA.

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Introduction

Food allergy to wheat results in various clinical symptoms. Atopic dermatitis occurs in children, whereas severe allergic reactions, such as wheat-dependent exercise-induced anaphylaxis (WDEIA), are commonly found in adults [1]. To diagnose WDEIA, an exercise challenge test following wheat ingestion should be performed. However,

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Table 1. Clinical features and immunological findings of the study subjects

	Patient No.	Age years	Gender	Diagnosis	Total IgE kU/l	Specific IgE to wheat, kU/l	Specific IgE to ω -5 gliadin, kU/l	Associated allergic diseases
Group 1 (n = 17)	1	64	M	WIA	1,773	2.19	20.30	CU, AR, AC
	2	35	M	WIA	76	<0.35	5.87	none
	3	39	M	WIA	383	0.49	3.76	AR
	4	48	M	WIA	85	<0.35	3.39	none
	5	56	M	WDEIA	261	<0.35	3.09	CU
	6	31	M	WDEIA	415	7.78	26.70	AR
	7	39	M	WDEIA	368	0.86	9.71	AR, AC
	8	33	F	WDEIA	99	0.40	4.77	AR, AC
	9	22	M	WDEIA	254	<0.35	10.60	AR, seafood allergy
	10	53	F	WDEIA	49	<0.35	1.69	AR, AC, CU
	11	44	M	WDEIA	115	<0.35	1.62	none
	12	27	M	WDEIA	224	<0.35	2.59	AR, AC
	13	41	F	WDEIA	190	0.53	1.82	NAR, drug allergy
	14	30	M	WDEIA	44	<0.35	3.82	CU, AR, AC
	15	15	M	WDEIA	73	<0.35	0.69	NAR
	16	28	M	WDEIA	386	2.58	7.44	none
	17	42	M	WDEIA	34	0.84	10.80	none
Group 2 (n = 10)	1	56	M	U	834	0.67	1.32	drug allergy, AR, AC
	2	25	M	U	107	0.61	<0.35	AR, AC, BA
	3	26	F	AP	>5,000	15.6	1.35	AR, AC, AD, BA
	4	16	M	AD	380	4.88	<0.35	AR, AC, AD
	5	20	M	AD	>5,000	0.38	<0.35	AD
	6	41	M	U	372	1.76	<0.35	CU
	7	37	M	U	1,113	1.10	<0.35	CU
	8	37	F	U	1,912	1.17	<0.35	CU
	9	72	M	U	1,121	1.54	<0.35	CU, bee sting anaphylaxis
	10	24	M	U	60	1.55	<0.35	AR, OAS

Group 1: patients with WDEIA or WIA; group 2: patients with other wheat allergies. AC = Allergic conjunctivitis; AD = atopic dermatitis; AP = abdominal pain; AR = allergic rhinitis; BA = bronchial asthma; CU = chronic urticaria; NAR = nonallergic rhinitis; OAS = oral allergy syndrome; U = urticaria.

er, the provocation test is time-consuming and unsafe, because the amount of food and the degree of exercise varies and anaphylactic shock often occurs. Thus, an in vitro diagnostic test for predicting severe systemic reactions is desirable.

The compound ω -5 gliadin has been identified as a major allergen for adult patients with WDEIA [2], as well as children with wheat-induced anaphylaxis (WIA) [3]. In clinical practice, immunoglobulin E (IgE) specific to wheat or ω -5 gliadin can be measured using the ImmunoCAP system (Phadia, Uppsala, Sweden) [4].

Although the clinical usefulness of IgE specific to ω -5 gliadin in WDEIA has been reported [2], there are no data regarding serum IgE to wheat or ω -5 gliadin allergens with regard to the various clinical manifestations of wheat allergy. Thus, we evaluated the diagnostic value of

serum IgE specific to wheat and to ω -5 gliadin in adult patients with wheat allergy for distinguishing severe allergic reaction from other types of allergies.

Patients and Methods

Based on their medical history and laboratory tests, 27 adult patients with allergic symptoms after the ingestion of wheat-containing foods were enrolled. The patients were classified into 2 groups according to the severity of their allergic reactions to wheat. Group 1 included 13 patients with WDEIA and 4 patients with WIA who had visited the emergency room due to anaphylaxis and had shown high serum tryptase levels. Group 2 consisted of 10 patients having urticaria or an acute exacerbation of atopic dermatitis with no episodes of anaphylaxis.

Sera from patients were tested for serum IgE specific to wheat and to ω -5 gliadin using the ImmunoCAP system (Phadia). Posi-

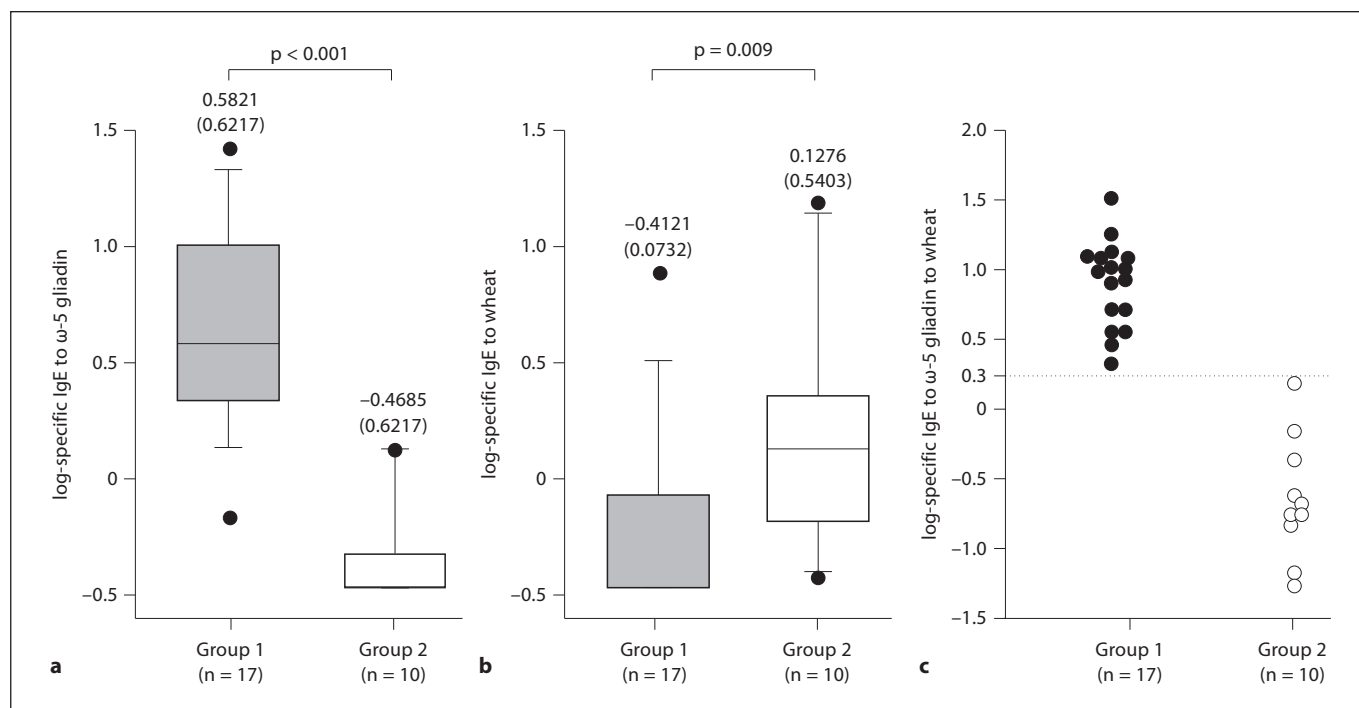


Fig. 1. Comparison of log-transformed specific IgE to ω-5 gliadin (a), wheat (b) and the ratio of ω-5 gliadin to wheat (c) in subjects with WDEIA or WIA (group 1) and other wheat allergies (group 2). Numerical data reported in the figure are median and interquartile range (parentheses). The dotted line indicates the log-transformed cutoff value of ω-5 gliadin/wheat.

tive results were defined as levels ≥ 0.35 kU/l based on the manufacturer's guidelines. When patients showed values < 0.35 kU/l, we treated the result as 0.34 to compare data between the 2 groups. Before statistical analysis, serum IgE data were converted to log IgE values because IgE levels were not normally distributed.

Serum IgE levels specific to wheat and to ω-5 gliadin of the 2 groups were compared using a Mann-Whitney U test. Statistical significance was indicated by p values < 0.05 . To evaluate the diagnostic value of serum IgE specific to wheat and to ω-5 gliadin, receiver operator characteristic (ROC) curves were prepared. Sensitivity and specificity were calculated according to the identified optimal cutoff. Statistical analyses were performed using the SPSS software (ver. 16.0; SPSS, Inc., Chicago, Ill., USA).

Results

Clinical features and laboratory findings from the study subjects are summarized in table 1. Serum IgE specific to wheat showed positive responses in 47% (8/17) of group 1 patients and 100% (10/10) of group 2 patients. However, all patients (100%) in group 1 showed positive responses to IgE specific to ω-5 gliadin compared with

only 20% in group 2. The log-transformed median value and interquartile range of IgE to wheat and to ω-5 gliadin are shown in figure 1.

To identify a better diagnostic value, the log-transformed specific IgE ratio of ω-5 gliadin to wheat was calculated and a cutoff value of 0.3 (two of the original raw values of IgE specific to ω-5 gliadin/wheat) was derived from the ROC curve. This measure was found to have 100% sensitivity and specificity, which was more useful than individual specific IgE levels (fig. 1). Using wheat-specific IgE levels (≥ 0.35 kU/l), the sensitivity was only 53%. Finally, using ω-5 gliadin-specific IgE levels (≥ 0.35 kU/l) sensitivity increased to 100%, but specificity decreased to 80%.

Discussion

We identified the utility of the ratio of IgE specific to ω-5 gliadin versus wheat in the diagnosis of WDEIA and WIA compared with other types of clinical allergies to

wheat. Food allergy after wheat ingestion appears to be rare in adulthood. In some cases, it may lead to exacerbation of atopic dermatitis and gastrointestinal symptoms. A unique form of allergy, WDEIA, develops predominantly in young adults and adolescents [5]. A few cases of WIA, which were enhanced by aspirin or nonsteroidal anti-inflammatory drugs, have been reported in adult patients [6, 7]. We identified 4 adult patients with WIA in this study. Without any medication or exercise, the patients had anaphylactic reactions after the ingestion of foods made with wheat. They showed strong positive specific IgE responses to ω -5 gliadin allergens, but not to wheat, indicating that ω -5 gliadin is the causative allergen in adults with WIA.

Regarding the allergens involved in wheat food allergies, allergic responses to wheat ingestion can be divided into two clinical phenotypes (WDEIA, WIA) and other symptoms. Severe allergic reactions, such as WDEIA or WIA, are primarily associated with ω -5 gliadin or high-molecular-weight glutenin subunits. Other responses are related to a wide range of water and salt-soluble and insoluble wheat proteins [7, 8]. Nevertheless, the measurement of ω -5 gliadin does not always predict severe allergic reactions. In a previous study, 78% of patients with WDEIA had detectable IgE specific to ω -5 gliadin [4]. In cases of wheat allergy, using the cutoff value of IgE specific to wheat allergen showed 61% sensitivity and 94% specificity for the diagnosis of wheat allergies [9]. In this

study, 47% of group 1 showed positive results to wheat allergen; however, 100% of group 2 subjects showed positive results to wheat allergen, while only 20% of these patients were sensitized to ω -5 gliadin allergens.

Thus, we measured both IgE specific to wheat and to ω -5 gliadin in the sera of patients and calculated the ratio in comparison with the clinical features of wheat allergy. Using a specific cutoff value of 0.3, we found 100% sensitivity and specificity distinguished patients with severe wheat allergy, such as WDEIA or WIA, from patients with other forms of wheat allergies in our study population. Considering the risk of food challenge tests in patients with a history of anaphylaxis, in vitro tests using ImmunoCAP are a useful method in clinical practice.

In conclusion, this study confirms that the serum IgE-specific ratio of ω -5 gliadin to wheat has the highest sensitivity and specificity. We suggest that this ratio could be a useful marker for the diagnosis of WDEIA and WIA in adult patients without undertaking food challenge tests.

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