

Which cereal is a suitable substitute for wheat in children with wheat allergy?

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Wheat is one of the main food allergens. It is among widely used cereals and there is an extensive cross-reaction between cereals. The aim of this study is to evaluate the extent to which cereals cross-react and to find the best substitute for wheat. Eighteen patients with definite diagnosis of type I hypersensitivity reactions to wheat enrolled in this study. Measurement of serum-specific IgE and skin prick test (SPT) for cereals flour (wheat, barley, oat, rye, rice and corn) and wheat bran was carried out. Also, open food challenge tests with available and conventional cereals in Iranian food culture (wheat, corn, rice and barley) were carried out. The SPTs were positive in 44.4% of patients for barley, 94.5% for wheat and 44–77% for other cereals. Positive serum-specific IgE was remarkable for wheat and barley and there was correlation between wheat and barley-specific IgE concentrations ($r = 0.773$ and $p < 0.01$). Corn serum-specific IgE was measured in 10 patients, which were positive in six of them. Of the patients, 55.5% had positive barley challenge tests, but all corn and rice challenge tests were negative. The best substitutes for wheat in wheat allergic patients are rice and corn. Regarding the correlation of wheat and barley serum-specific IgEs, there might be a high antigenic cross-reaction, therefore barley is not a good substitute for wheat and consuming barley needs a careful challenge test. Considering concordance of positive SPT to wheat flour and wheat bran, avoiding both of them is necessary in patients with wheat allergy.

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Cereal families, including wheat, barley, oat, rye, rice, and corn are food materials produced and consumed in large quantities all over the world (1). Wheat is a major nutrient source and is among the six major foods that account for food hypersensitivity in children (2).

Wheat allergy may present with cutaneous, respiratory, and gastrointestinal manifestations and may be severe and life threatening in some patients (3). Although there are some similarities between wheat allergy, as an IgE-mediated food allergy, and other adverse reactions to wheat such as baker's asthma, celiac disease, and wheat-dependent exercise-induced anaphylaxis, differences are present in the specific allergens, the patterns of exposure to allergens, immunologic mechanisms, and pathophysiology (2).

Different reports about the cereals cross-reactions have been published. In a group of patients with positive double-blind placebo-controlled food challenge, a great cross-reaction was observed between cereals. Also, the cross-reaction between wheat, barley, and oat has been seen in RAST (4). Wheat has 40 different antigens of which half cross-react with rye antigens (5).

This research was designed to study the cross-reactions between cereals and to identify a suitable substitute for wheat in wheat allergic patients.

Materials and methods

In this prospective study, 18 wheat-allergic patients, aged between 1 and 8 yr old, 12 boys and six girls, were evaluated for allergy to other

cereals. The mean and one standard deviation of the patients' age were 2.6 ± 1.7 yr old. The diagnosis of wheat allergy was confirmed if the patients had at least one of the following criteria:

- 1 A definite history of type I hypersensitivity reactions following the ingestion of wheat, in addition to a positive wheat skin prick test (SPT) and/or serum-specific IgE.
- 2 A history of anaphylaxis following the ingestion of wheat.
- 3 Positive wheat challenge test.

The following tests were performed to diagnose allergy to other cereals, to clarify the cereals cross-reaction and to find the best cereal substitute in wheat allergic patients:

- 1 SPT: All the patients underwent SPT with wheat bran and wheat, barley, corn, rice, oat, and rye flours, except those with acute symptoms or a history of anaphylaxis during the recent month, in whom this test was delayed until they had recovered. A positive (histamine dihydrochloride 1 mg/ml) and a negative control (normal saline) were also included in the test. The SPT responses were read for histamine at 10 min and for allergens at 20 min and were considered positive for histamine if the diameter of the wheal was at least 5 mm and for allergens at least 3 mm larger than the reaction to the negative control. The extracts were obtained from Dome Holister Stier (Miles, Canada).
- 2 Measurement of serum-specific IgE: After sampling 1 ml of peripheral blood, sterile serum was separated and immediately frozen in -80°C . Serum-specific IgE for wheat, barley, corn, rice, oat, and rye were measured using the ELISA method (Clonesystems Company, Hamburg, Germany). According to the kit manual the results were categorized into seven groups (class 0–6). The results equal to class 1 or more were considered positive. Wheat, barley, rice, oat, and rye serum-specific IgEs were measured in all patients but corn serum-specific IgE was measured only in 10 patients.
- 3 Oral Challenge Test (with three conventional cereals in Iran; barley, corn, and rice): although double-blind placebo-controlled food challenge is the gold standard for diagnosing food allergy, in infants and young children (especially under 3 yr of age) whose allergy symptoms are predominantly objective and the effect of suggestion is minimal, open food challenge test seems suitable to prove food allergy (6, 7). The patients were

advised not to take antihistamines for a certain period of time before provocation, based on the type of the antihistamine (8). All the patients underwent challenge tests with barley, corn, and rice, in their boiled form, in different sessions with 20–40-day intervals. Each patient came to our clinic early in the morning in fasting state, where all emergency equipment was at hand. Before the challenge test, a complete physical examination was carried out for every patient. If there were any sign or symptom of allergy, which could alter the results of the study such as skin lesions, wheezing, and rhinitis, the food challenge test was canceled. The amount of the food for the challenge test was determined to be almost equal to the mean daily intake, according to the patients' age and weight. The food for the challenge test was divided into five parts. The time interval between having the parts was 30 min. The patients were under close observation. The results of the food challenge were considered positive by a pediatric allergy specialist, if one or more of the following objective clinical reaction(s) were noted: urticaria, angioedema, wheezing, cough, dyspnea, vomiting, diarrhea, abdominal pain, exacerbation of eczema, or anaphylactic shock. At the end of the challenge test, the patient was observed for 4–8 h. If the patient had any clinical reaction during the test, it was stopped and medical interventions were employed, then the patient was observed for 6–12 h or as an inpatient. The patients were advised to record and report any symptoms they experienced after discharge during the first day, or return to hospital if they had severe symptoms.

Statistical analysis

Pearson correlation test was used to evaluate the correlation between wheat and other cereals serum specific IgE concentrations.

Results

In this study 18 patients with definite diagnosis of wheat allergy were evaluated for allergy to other cereals. All the patients had positive wheat SPT and wheat serum-specific IgE was positive in 17 patients (94.5%). The results of SPT for wheat flour and wheat bran are compared in Fig. 1. All the patients had positive SPT for wheat bran and wheat flour.

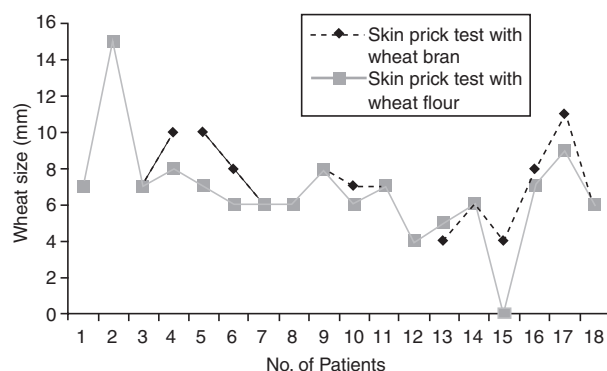


Fig. 1. Comparison of wheat bran and wheat flour skin prick test.

Barley, corn, rice, oat, and rye SPT were positive in eight (44.4%), 10 (55.5%), 9 (50%), 14 (77.7%), 14 (77.7%) patients respectively. Positive serum-specific IgE was seen in 17 patients (94.5%) for wheat, 16 (88.8%) for barley, seven (70%) for corn (all below class 3), four (22.2%) for rice, nine (50%) for oat and one (5.5%) for rye. There was a correlation between wheat and barley-specific IgE concentration ($r = 0.773$, $p < 0.01$), but no correlation was observed between specific IgEs for wheat and corn ($r = 0.64$, $P > 0.8$), rice ($r = 0.31$, $P > 0.2$),

oat ($r = 0.18$, $P > 0.4$), and rye ($r = 0.41$, $P > 0.08$).

The clinical manifestations of the hypersensitivity after normal ingestion and also challenge tests, the onset time after ingestion, the evoking dosages and the cooking style for wheat and barley are summarized in Table 1. Excluding the patients with anaphylaxis following ingestion of wheat and those with a definite history of type I hypersensitivity reactions following the ingestion of wheat in addition to a positive wheat SPT and/or specific IgE (the diagnosis of wheat allergy is definite in these groups and the challenge test is dangerous and also superfluous), wheat challenge test was performed in three patients that was positive in all of them. Ten patients (55.5%) had positive barley challenge tests. No hypersensitivity reaction to rice and corn was noted following the ingestion of them.

Discussion

Rice and corn are suitable substitutes for wheat in patients with wheat allergy, as all of the patients in this study had negative rice and corn challenge tests. Positive rice and corn SPTs in some of the patients may be the result of high

Table 1. The clinical manifestations of the patients after ingestion and challenges of wheat and barley, the cooking styles of them, the evoking dosages, and the onset time of manifestations after ingestion in wheat allergic patients

No.	Clinical Manifestations					Cooking style				Evoking dosages (In challenge)	
	Wheat		Barley		The onset after ingestion (min)	Wheat		Barley		Wheat	Barley
	After ingestion	After challenge	After ingestion	After challenge		Primary ingestion	For challenge	Primary ingestion	For challenge		
1	C, R, A		R	R	<30	Pre-cooked cereal		Boiled	Boiled		5th part
2	C, A		C, R	R	<30	Baked		Boiled	Boiled		1st part
3*	C, R	C, R	†	—	<30	Boiled	Baked		Boiled	1st part	
4	C, R, G, A		†	—	<30	Pre-cooked cereal			Boiled		
5	C		†	—	<30	Baked			Boiled		
6	C, R, G		†	G	<30	Baked			Boiled		3rd part
7	C, R, A		S	—	<30	Baked		Boiled	Boiled		
8	C, A		C, R	C, R	<30	Baked		Boiled	Boiled		3rd part
9	C, R, A		C	C	<30	Baked		Boiled	Boiled		1st part
10	C, G, A		C	C	<30	Baked		Boiled	Boiled		1st part
11	C, R, A		†	—	<30	Pre-cooked cereal			Boiled		
12	C, A		†	—	<30	Baked			Boiled		
13	C, R, G, A		R	—	<30	Pre-cooked cereal		Boiled	Boiled		
14	C, G		C	C	<30	Pre-cooked cereal		Boiled	Boiled		1st part
15*	C	C	†	—	<30	Baked	Baked		Boiled	3rd part	
16	R, G, A		C, G	C, G	<30	Baked		Boiled	Boiled		1st part
17*	C, R	C, R	C	C	<30	Baked	Baked	Boiled	Boiled	5th part	1st part
18	G, A		C	C	<30	Baked		Boiled	Boiled		1st part

C, cutaneous symptoms, G, gastrointestinal symptoms, R, respiratory symptoms, A, Anaphylaxis.

*Wheat challenge test was carried out.

†They had not ingested barley before challenge test.

false positive results in SPT (9) or because of the antigenic cross-reaction between cereals and grasses (10). Also, of the patients 70% had positive corn-specific IgE but all of them had negative challenge tests. Corn serum-specific IgE in all of them was below class 3, which may be too low to induce allergy symptoms and it should be emphasized that only 30–40% of the patients with positive specific IgE for food allergens show clinical manifestations of food allergy (11).

No significant difference was noted between the results of SPTs for wheat flour and wheat bran, therefore avoiding both of them is necessary in patients with wheat allergy. In a study by Baldo et al. (12) on the serum of patients with baker's asthma, wheat bran was reported to be at least as allergenic as wheat flour, but baker's asthma and wheat allergy as a food allergy are completely different in the specific allergens, patterns of allergen exposure, immunologic mechanism and pathophysiology (2).

Evaluation of serum-specific IgE has been reported as an appropriate way to identify the cross-reactions between cereals, although exact identification of the cross-reactions needs more laboratory evaluations (10). According to the results of this study, there was a correlation between wheat and barley-specific IgEs, so there may be a high antigenic cross-reaction between wheat and barley. Also, 55.5% of the patients with wheat allergy had positive barley challenge tests. Regarding the acute reactions observed in barley challenge tests, avoiding barley consumption is suggested to patients with wheat allergy, unless there is a negative barley challenge test.

Considering the discrepancy between rye SPT (positive in 77.7% of patients) and rye-specific IgE (negative in almost all of our patients), it seems despite our accuracy in the measurement of rye-specific IgE, the test was not working. It has been reported that half of wheat antigens have cross-reaction with rye antigens (5). Oat SPT and serum-specific IgE were also positive in a remarkable number of patients. Therefore, oat and rye are recommended to pass challenge tests and be substituted for wheat if the challenge tests were negative.

Cereal grains are taxonomically classified in the Poaceae family. Wheat, barley, oat, and rye belong to the Festucoideae subfamily, but rice and corn belong to other subfamilies (Oryzoideae and Panicoideae, respectively) (10). According to the results of this study, a considerable number of wheat allergic patients

had also allergic reactions to barley, but none of them had allergic reactions to rice and corn, which might be the result of their taxonomical relationship.

Finally, rice and corn are recommended as suitable substitutes for wheat in patients with wheat allergy. Rice and corn could be used to bake bread and cake with good quality. Rye and oat should undergo more evaluation, especially challenge tests. Rye could be employed for baking bread but oat bread does not have a good quality (13). Considering that 55.5% of the patients had positive barley challenge tests and the concordance of wheat and barley-specific IgEs, substituting wheat with barley is not recommended, unless there is a negative barley challenge test.

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