



REVIEW ARTICLE

What You Need To Know About Wheat Allergy and Wheat Dependent Exercise Induced Anaphylaxis

Iman Hamed Nasr¹, Humaid Al Wahshi²

Immunology and allergy unit, Royal hospital, Muscat, PC 116, PO Box 546, Oman.

Rheumatology unit, Royal hospital, Muscat, PC 116, Po Box 546, Oman.

Abstract

Wheat allergy is the most common of the cereal grain allergies. It is caused by immunologic responses to a range of different proteins in wheat. These can be divided into Immunoglobulin E (IgE)- mediated (immediate) and/or non IgE-mediated (delayed) allergic reactions. Wheat allergy presents with a wide range of symptoms and manifestations such as exacerbation of atopic dermatitis, wheat dependent exercise-induced anaphylaxis, eosinophilic esophagitis (EoE), baker's asthma, and celiac disease. In IgE mediated reactions, symptoms include the skin and mucus membranes, respiratory system, gastrointestinal system and cardiovascular system. Wheat dependent exercise-induced anaphylaxis is a form of IgE mediated allergy to wheat proteins that occurs only if wheat ingestion is followed by exercise and not if wheat is ingested without exercising. Diagnosis of IgE mediated wheat allergy includes In vivo skin test, In vitro test and oral food challenge testing. Avoidance of wheat is the mainstay of treatment in wheat allergy. Avoiding eating wheat and foods containing wheat 4- 6 hours prior to exercise is advised in patients with wheat dependent exercise-induced anaphylaxis. In this article, we will focus on the IgE mediated (immediate) allergic reaction and wheat dependent exercise-induced anaphylaxis, pathogenesis, diagnosis and management.

Keywords: Wheat allergy, WDEIA, omega 5 gliadin, component testing, epinephrine auto injector

Wheat allergy

Wheat allergy is the most common grain allergy. IgE-mediated (immediate) wheat allergy is estimated to affect 0.2 to 1.3% of children in Europe and 0.4% of children in the US [1,2]. Symptoms develop within minutes and rarely upto 2 hours of ingestion of wheat. Specific IgE to one or more wheat proteins (globulins and albumins, glutenins and gliadins) is formed [3,4]. This then leads to the release of vasoactive mediators from mast cells and basophils resulting in allergic symptoms that may affect the skin and mucus membranes such as itching, rash, angioedema or exacerbation of atopic dermatitis, the respiratory system as chest tightness, wheeze and difficulty in breathing, the gastrointestinal system including abdominal pain, nausea and/or diarrhea, and the cardiovascular system with tachycardia, hypotension and collapse. Allergy to wheat can lead to life threatening reactions (also known as anaphylaxis) and death even if small amounts were ingested. Inhalation of wheat proteins is responsible for the respiratory symptoms in occupational and household wheat exposures such as in Baker's asthma and touching can cause localized urticaria. Wheat dependent exercise-induced anaphylaxis (WDEIA) is a condition where anaphylaxis is triggered by exercise within minutes to a few hours after the ingestion of foods containing wheat. This does not happen when wheat is eaten in the absence of exercise nor with exercise alone. Symptoms may begin at any stage of exercise and include warmth, flushing, itching, urticaria, angioedema, abdominal

pain, nausea, vomiting, diarrhea, laryngeal edema, hypotension and collapse. The majority of patients exercises regularly but experience attacks only occasionally and is unpredictable. A minority experience symptoms during most attempts at exercise. In most cases vigorous exercise trigger WDEIA, however, there are reported cases of milder forms of exercise such as walking [5]. The mechanism is not fully understood. Increased gastric permeability can increase during exercise, which increases the entry of intact or incompletely digested allergens into the circulation during exercise but not during rest [6,7]. Another possible explanation is that omega-5 gliadin-derived peptides are cross-linked with tissue transglutaminase (tTG), which leads to an increase in IgE antibody binding and the formation of large allergen complexes responsible for eliciting anaphylactic reactions [8].

Diagnosis of IgE mediated wheat allergy

Diagnosis is important as strict avoidance of wheat and all foods containing it is the mainstay of treatment. Diagnosis usually starts with a detailed clinical history of the reaction. In vivo and in vitro tests are available to support (but not exclude) the diagnosis of wheat allergy. In vivo testing is done by skin

Correspondence to: Iman Hamed Nasr, Immunology and allergy unit, Royal hospital, Muscat, PC 116, PO Box 546, Oman. E-mail: drimannasr[AT]gmail[DOT]com

Received: Dec 19, 2017; **Accepted:** Dec 21, 2017; **Published:** Dec 24, 2017

prick test to wheat. Commercial wheat extract or fresh wheat is used for the skin prick test. Histamine and normal saline serve as positive and negative controls for the test. A drop of the wheat extract is applied on the skin and pricked with a plastic lancet. After 15-20 minutes, the skin is examined for redness and a wheal. A positive skin prick test is defined as a wheal with the diameter measuring 3 mm more than the negative control. Patients need to be off antihistamines for at least 5 days prior to the test in order to avoid false negative results. In vitro testing measures specific IgE antibodies to wheat in the serum. Skin testing is preferred over In vitro testing as it has good sensitivity and specificity (92% and 84% respectively) [9]. In vitro testing has a low positive predictive value since it also measures IgE antibodies to grass pollen due to the shared IgE epitope with wheat. In addition, it does not measure all proteins in wheat such as omega-5 gliadin which is a protein component in gluten responsible for severe allergic reactions as well as wheat dependent exercise-induced anaphylaxis (WDEIA) [10]. Measuring IgE to defined allergen rather than the whole extract overcomes this problem. This is done through a commercial assay called component resolved testing (Immuno CAP, Thermo Fisher Scientific). Serum IgE to recombinant omega-5 gliadin is available and may be positive even when IgE to wheat is negative [11]. The gold standard for diagnosis of IgE mediated wheat allergy is an oral food challenge (OFC). This can be done as an open challenge or in certain cases a double-blind, placebo-controlled oral food challenge (DBPCFC) when skin testing as well as component resolved testing is negative but the clinical suspicion is still high. It must be performed by an allergist in a setting with resuscitation facilities.

Management

Strict dietary avoidance of wheat and foods containing it is the crucial step in the management of wheat allergy. Patients should be supported by experienced dietitians. In wheat dependent, exercise-induced anaphylaxis (WDEIA) patients should avoid any foods containing wheat for at least four to six hours before exercise with the help of the dietitian. All patients with WDEIA should carry an epinephrine auto injector for self-injection in case of anaphylaxis and should be counseled on when and how to use it. Patients must be aware of early symptoms such as flushing, itching, difficulty breathing and must stop exercising immediately if any of these occur and to self-administer epinephrine intramuscularly if needed. They should be advised not to exercise alone and to educate their sports mate on how to use the epinephrine auto injector when needed. Non-sedating second generation antihistamines taken daily 2 hours prior to exercising may help reduce the symptoms. A trial of high dose cromoglycates (cromolyn sodium) taken orally 100 mg in children and 200 mg in adults 20 minutes before eating may be useful in preventing attacks in a few case studies [12-14]. However, they should be advised

not to rely on these medications to prevent attacks as despite these anaphylaxis may occur.

References

- Venter C, Pereira B, Grundy J (2006) Incidence of parentally reported and clinically diagnosed food hypersensitivity in the first year of life. *J Allergy Clin Immunol* 117: 1118-24. [[View Article](#)]
- Gupta RS, Springston EE, Warrier MR (2011) The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics* 128: e9-17. [[View Article](#)]
- Battais F, Pineau F, Popineau Y (2003) Food allergy to wheat: identification of immunoglobulin E and immunoglobulin G-binding proteins with sequential extracts and purified proteins from wheat flour. *Clin Exp Allergy* 33: 962-70. [[View Article](#)]
- Pastorello EA, Farioli L, Conti A (2007) Wheat IgE-mediated food allergy in European patients: alpha-amylase inhibitors, lipid transfer proteins and low-molecular-weight glutenins. Allergenic molecules recognized by double-blind, placebo-controlled food challenge. *Int Arch Allergy Immunol* 144: 10-22. [[View Article](#)]
- Pérez-Rangel I, Gonzalo-Garijo MA, Pérez-Calderón R (2013) Wheat-dependent exercise-induced anaphylaxis in elderly patients. *Ann Allergy Asthma Immunol* 110: 121-3. [[View Article](#)]
- Matsuo H, Morimoto K, Akaki T (2005) Exercise and aspirin increase levels of circulating gliadin peptides in patients with wheat-dependent exercise-induced anaphylaxis. *Clin Exp Allergy* 35: 461-6. [[View Article](#)]
- Yano H, Kato Y, Matsuda T (2002) Acute exercise induces gastrointestinal leakage of allergen in lysozyme-sensitized mice. *Eur J Appl Physiol* 87: 358-64. [[View Article](#)]
- Palosuo K, Varjonen E, Nurkkala J (2003) Transglutaminase-mediated cross-linking of a peptic fraction of omega-5 gliadin enhances IgE reactivity in wheat-dependent, exercise-induced anaphylaxis. *J Allergy Clin Immunol* 111: 1386-92. [[View Article](#)]
- Le TA, Al Kindi M, Tan JA (2016) The clinical spectrum of omega-5-gliadin allergy. *Intern Med J* 46: 710-6. [[View Article](#)]
- Morita E, Matsuo H, Chinuki Y (2009) Food-dependent exercise-induced anaphylaxis-importance of omega-5 gliadin and HMW-glutenin as causative antigens for wheat dependent exercise-induced anaphylaxis. *Allergol Int* 58: 493-8. [[View Article](#)]
- Ito K, Futamura M, Borres MP (2008) IgE antibodies to omega-5 gliadin associate with immediate symptoms on oral wheat challenge in Japanese children. *Allergy* 63: 1536-42. [[View Article](#)]
- Juji F, Suko M (1994) Effectiveness of disodium cromoglycate in food-dependent, exercise-induced anaphylaxis: a case report. *Ann Allergy* 72: 452-4. [[View Article](#)]
- Sugimura T, Tananari Y, Ozaki YY (2009) Effect of oral sodium cromoglycate in 2 children with food-dependent exercise-induced anaphylaxis (FDEIA). *Clin Pediatr (Phila)* 48: 945-50. [[View Article](#)]
- Ueno M, Adachi A, Shimoura S (2008) A case of wheat-dependent exercise-induced anaphylaxis controlled by sodium cromoglycate, but not controlled by misoprostol. *J Environ Dermatol Cutan Allergol* 2: 118-22. [[View Article](#)]

Citation: Nasr IH, Al Wahshi HA (2017) What You Need To Know About Wheat Allergy and Wheat Dependent Exercise Induced Anaphylaxis. *J Nutr Diet Pract* 1: 001-002.

Copyright: © 2017 Nasr IH, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.