doi:10.1594/eaacinet2007/EO/6-300507 http://www.eaaci.net

ROLE OF FOOD IN URTICARIA

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doi:10.1594/eaacinet2007/EO/6-300507 http://www.eaaci.net

INTRODUCTION

In urticaria, adverse reactions to food are only a frequent finding in the subset of patients with chronic continuous urticaria. Mostly these reactions are of pseudoallergic nature, directed against artificial additives as well as naturally occurring aromatic components. IgE-mediated allergic reactions are a rare cause in acute urticaria as well as in recurrent chronic urticaria. In other types of urticaria, e.g. physical urticaria, food plays hardly any role as an eliciting agent with the exception of ice-cold drinks in cold urticaria. By contrast, exercise-induced anaphylaxis is frequently food-dependent. Two subtypes are distinguished: unspecific food-dependent exercise-induced anaphylaxis (FDEIA), where the filling of the stomach independently of the kind of food ingested prior to exercise is responsible for the symptoms. In specific FDEIA, an IgE-mediated food allergy causes symptoms only in combination with exercise. In the latter group, wheat is an important allergen.

Urticaria is characterized by the occurrence of wheals and in some cases angioedema. Wheals are defined by a surrounding reflex erythema, associated itching and the fleeting nature (persistence of the wheal < 24 h). Urticaria is the heading for a heterogeneous group of distinct entities. These subgroups are characterized by disease duration, pathogenesis, eliciting agents and clinical features. In order to compare results from different studies it is of highest importance to differentiate clearly among the various subtypes and to adhere to the consensus classification of urticaria [1].

Exercise-induced anaphylaxis (EIA) is characterized by airway obstruction, urticaria and hypotension following physical exercise. A subtype of EIA related to the intake of specific food is known as food-dependent, exercise-induced anaphylaxis (FDEIA). In some cases, specific foods cause anaphylaxis when exercise follows ingestion, but are tolerated if no exercise follows ingestion. (specific FDEIA).

Data concerning food as an eliciting factor in urticaria are limited due to difficulties in the diagnosis of food allergy and especially of food pseudoallergy with the necessity of double-blind, placebo-controlled food challenge (DBPCFC); and due to the fact that not only the elicitation of wheals but also the augmentation of disease activity needs to be kept in mind.

ACUTE URTICARIA

Acute urticaria is a common disease affecting approximately 15–23% of the population at least once in their lifetime [2]. Patient's history is important but often unreliable since the role of food is generally overestimated; 63% of patients with acute urticaria suspect food as an eliciting factor [2]. In acute urticaria IgE-mediated adverse reactions to food have been confirmed in less than 1% of patients [2, 3], whereas in recurrent episodes of acute whealing this rate was reported to be higher in the past (10%) [3a]. In general food appears to be of higher importance for acute urticaria in early childhood. Here, in up to 15% IgE-mediated reactions were reported in the age group from 6 months to 16 years [4]. Pseudoallergic reactions against food were not reported in any of these studies, but pseudoallergic reactions against NSAID are reported to be the second most frequent cause, responsible for 9% of acute urticaria cases. An upper respiratory tract infection [5] was identified as the most frequent cause.

CHRONIC URTICARIA

As with acute urticaria, type I-allergic reactions were rarely reported to be responsible for the development of chronic urticaria [2, 6]. However, a type I allergy should be ruled out in those patients who suffer from intermittent attacks of whealing lasting for a few hours only, shortly after the ingestion of food. By contrast, in adult patients with chronic continuous urticaria with daily whealing a type I-allergic mechanism is unlikely, as the eliciting allergens would have to be ingested several times daily. In this subset of patients, pseudoallergic reactions to food and food additives have, in the past, been discussed separately from

infectious or autoimmune etiology due to the distinct nature of this reaction. The clinical symptoms of pseudoallergy cannot be clearly distinguished from a type I-allergic reaction. They occur often with a latency of more than 4 h and cease only after a prolonged omission of the suspected pseudoallergen for more than 10–14 days [5]. This is in contrast to type I allergies where the symptoms generally appear after 0–120 min and clear after a few hours or at the latest after 24–48 h. These aspects of pseudoallergy should also be kept in mind in interpreting different studies. Few studies have used the gold standard of DBPCFC tests; in some of the mentioned studies, elimination diets were only adhered to for a few days. Results may also differ due to heterogeneous study populations and study conditions. Some studies have included not only patients with chronic urticaria but also patients with physical urticaria. In addition, approximately 50% of patients do not show a complete clearance of symptoms but have an improvement in disease intensity, which indicates the involvement of cofactors. Finally, a study outcome may also depend on the country where the study was performed (e.g. parasitic infections are more frequent in developing countries, hepatitis B is more frequent in southern than in northern Europe) and on the variations in health systems. The latter is key, as none of the studies are cross-sectional population-based investigations, and in some countries referrals to specialists are only allowed in severe cases. In our own study [5] unselected patients with chronic continuous urticaria were included who had not previously received a diagnostic work-up. In this group a high incidence of pseudoallergic reactions to food was seen. Pigatto and Valsecchi [7] later confirmed these results in their investigation of a group of 202 patients with chronic urticaria, in which they used identical diet and study conditions.

DIAGNOSIS OF ADVERSE REACTIONS TO FOOD IN URTICARIA

The recommended diagnostic procedures in urticaria have been published in a recent consensus report [1]. A detailed description of adverse type 1 allergic reactions to food is given below in the section on diagnosis of FDEIA. For diagnosis of pseudoallergy as an eliciting factor, patients with chronic continuous urticaria should be given a diet low in pseudoallergens. Patients should be warned regarding potential pitfalls, providing recipes is regarded as helpful [8]. The diet

should be followed for at least 3 weeks and a detailed diary about the food eaten should be kept by the patient, to double-check for involuntary errors. This should be accompanied by a symptom protocol using a simple symptom score of 0–3 [1]. In case of symptom score improvement, a DBPCFC following the diet is the diagnostic gold standard for urticaria but difficult to perform on an outpatient basis.

FOOD-DEPENDENT EXERCISE –INDUCED ANAPHYLAXIS

Reports of FDEIA appear to be on the rise, possibly due to the increased popularity of exercise over the past decade [9]. However, only rare epidemiological data regarding the frequency of FDEIA in the general population are available. Aihara et al. [10] documented that the frequency of FDEIA in junior high school students in a Japanese school was !0.02%. Here, it must be noted that the mean age of FDEIA is between 25 and 35 years [11]. Because symptoms may vary, many people with FDEIA are often unaware of their condition and FDEIA remains undiagnosed [12]. Regarding the course of the disease, data are only available for EIA in general. Nancy et al. published a 10-year follow-up study with 365 US-American patients with EIA. 47% of those who answered a questionnaire stated that the frequency of attacks had decreased since primary onset. In 46% of patients the frequency of attacks had remained the same [11]. FDEIA was first reported by Maulitz et al. [14] in 1979. They described a case of a 31-year-old woman who developed anaphylaxis during long-distance running after eating shellfish. Since then, numerous foods have been implicated as causes of FDEIA. Shellfish, tomatoes and alcoholic drinks were the most frequent causes.

DIAGNOSIS OF FDEIA

If the patient's history suggests FDEIA, a thorough allergological work-up is mandatory. This should include specific IgE, skin prick testing with common inhalant allergens, possibly cross-reacting foods, as well as suspected foods. Prick-to-prick test with native allergens should be performed since this offers a high sensitivity [13]. Ultimately, a food challenge test followed by exercise is required for the confirmation of the diagnosis and must be performed in order to

avoid unnecessary diets or exercise restrictions. Provocation tests should be performed in the hospital due to the possibility of severe and sometimes delayed reactions. DBPCFC is the gold standard, but open challenge may be sufficient if no reaction occurs. However, it needs to be considered that some patients fail to develop clinical symptoms in provocation tests. False-negative test results may depend on the method of provocation. Suko et al. proposed that insufficient amounts of food allergen ingested or inappropriate exercise could result in false-negative clinical responses to challenge tests [15]. Hanakawa et al. [15] published a case of a young woman whose positive reaction to FDEIA depended on the amount of wheat allergen ingested. These authors concluded that an insufficient amount of food allergen ingested or subthreshold exercise levels may be reasons for unsuccessful challenge tests noted in several previous reports [15]. On the other hand, Aihara et al. [16] described a case of a 14-year-old boy who did not develop symptoms of FDEIA after ingestion of rice or ‘umeboshi’ (Japanese plum) alone but clearly after ingestion of the two foods together. In conclusion, a positive provocation test confirms clearly the diagnosis but a negative provocation test never completely rules out the presence of FDEIA in an individual [12]. In our own experience it is helpful to imitate the meals and amounts ingested if single food challenge is negative, although this is sometimes difficult to realize under DBPCFC conditions. If alcoholic beverages have been ingested they must included in the protocol, since they increase gastric allergen absorption and augment histamine release. Another eliciting factor may be associated drug intake, especially of drugs which enhance gastric mucosa permeability such as acetylsalicylic acid (ASA).

References

(01) Zuberbier T, Greaves M, Juhlin L, Lennart J, Kobza-Black A, Maurer D, Stingl G, Henz B: Definition, classification and routine diagnosis of urticaria: A consensus report. J Invest Dermatol Symp Proc 2001;6:123–127.

(02)Zuberbier T: The role of allergens and pseudoallergens in urticaria. J Invest Dermatol Symp Proc 2001;6:132–134.

(03)Aoki T, Kojima M, Horiko T: Acute urticaria: History and natural course of 50 patients. J Dermatol 1994;21:73–77.

(03a)Wüthrich B, Haecki-Hermann D: Zur Ätiologie der Urtikaria. Eine retrospektive Studie anhand von 316 konsekutiven Fällen. Z Hautkr 1980;55:102–111.

(04)Kauppinen K, Juntunen K, Lanki H: Urticaria in children. Retrospective evaluation and follow-up. Allergy 1984;39:469–472.

(05)Zuberbier T, Chantraine-Hess S, Hartmann K, Czarnetzki BM: Pseudoallergen-free diet in the treatment of chronic urticaria – A prospective study. Acta Derm Venereol 1995;75:484–487.

(06)Juhlin L: Recurrent urticaria: Clinical investigation of 330 patients. Br J Dermatol 1981; 104:369–381.

(07) Pigatto PD, Valsecchi RH: Chronic urticaria: A mystery. Allergy 2000;55:306–308.

(08) Henz BM, Zuberbier T, Grabbe J, Monroe E: Urticaria: Clinical, Diagnostic and Therapeutic Aspects. Berlin, Springer, 1998, pp 69–78, 196.

(09)Kutting B, Brehler R: Exercise-induced anaphylaxis. Allergy 2000;55:585–586.

(10). Aihara Y, Takahashi Y, Kotoyori T, Mitsuda T, Ito R, Aihara M, Ikezawa Z, Yokota S: Frequency of food-dependent, exercise-induced anaphylaxis in Japanese junior high school students. J Allergy Clin Immunol 2001;108:1035–1039.

(11)Shadick NA, Liang MH, Partridge AJ, Bingham C, Wright E, Fossel AH, Sheffer AL: The natural history of exercise-induced anaphylaxis: Survey results from a 10-year follow-up study. J Allergy Clin Immunol 1999;104:123–127.

(12) Hosey RG, Carek PJ, Goo A: Exercise-induced anaphylaxis and urticaria. Am Fam Physician 2001;64:1367–1372.

(13) Norgaard A, Skov PS, Bindslev-Jensen C: Egg and milk allergy in adults: Comparison between fresh foods and commercial allergen extracts in skin prick test and histamine release from basophils. Clin Exp Allergy 1992;22:940– 947.

(14)Maulitz RM, Pratt DS, Schocket AL: Exercise-induced anaphylactic reaction to shellfish. J Allergy Clin Immunol 1979;63:433–434

(15) Hanakawa Y, Tohyama M, Shirakata Y, Murakami S, Hashimoto K: Food-dependent exercise-induced anaphylaxis: A case related to the amount of food allergen ingested. Br J Dermatol 1998;138:898–900.

(16) Aihara Y, Kotoyori T, Takahashi Y, Osuna H, Ohnuma S, Ikezawa Z: The necessity for dual food intake to provoke food-dependent, exercise- induced anaphylaxis (FEIA): A case report of FEIA with simultaneous intake of wheat and umeboshi. J Allergy Clin Immunol 2001;107: 1100–1105.