

Buckwheat Allergy: An Emerging Clinical Problem in Europe

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Abstract

Buckwheat allergy is a clinical entity known since long time ago and frequent in Asia, where this crop is commonly eaten. In Europe, buckwheat allergy was an anecdotal description since few years ago, when the consumption of buckwheat dramatically increased together with the publication of case reports and case series of European patients with buckwheat allergy.

This review article describes and analyzes the history of buckwheat allergy, its clinical presentation, its increase in European countries during the last few years, and summarizes the main case reports, case series and epidemiological surveys on buckwheat allergy.

A summary of main buckwheat allergens and clinical relevant cross-reactivity are also described and discussed.

Background

Buckwheat (*Fagopyrum esculentum*) is a crop, taxonomically unrelated to wheat, of the *Polygonaceae* family. It is used to obtain dark gluten-free flour which can be used as supplement for patients with celiac disease. Buckwheat is also an important ingredient of several traditional Asian (i.e.: noodles like Japanese "soba" or Korean "naengyeon" noodles, jellies like Korean "memilmuk"), Russian (i.e.: pancakes called "blinis" or a sort of porridge called "kasha"), and European dishes (i.e.: French pancakes called "Breton galettes", Dutch "poffertjes", or Northern Italian hot porridge called "polenta taragna" and pasta called "pizzoccheri"). Buckwheat hulls are also used to fill pillows.

Despite the wide diffusion of traditional dishes made by buckwheat through European countries, the consumption of this crop, until few years ago, was limited to the small regions of each over-mentioned countries in which those characteristic dishes were traditionally eaten. In the last few years, the consumption of buckwheat in Europe dramatically increased (Figure 1) due to different and complex reasons (i.e.: the tendency to use buckwheat into mixes of flours to prepare pizza or bread [1,2], the increased diffusion of use of the so-called "minor cereals" through the network of "organic food shops", and a more ethnically diverse diet).

History of Buckwheat Allergy

Allergy to buckwheat is typically IgE mediated (only one case of Heiner Syndrome secondary to buckwheat allergy has been described so far [3]) and it is often associated to severe anaphylaxis [4].

The first description of a hypersensitivity reaction to buckwheat was published in 1909 by Smith H.L.: the described case was about patients who suffered from dyspnoea, acute rhinitis, urticaria and mucosal angioedema after the ingestion of buckwheat flour [5].

In 1926, Peshkin demonstrated for the first time a buckwheat positive skin prick test in an allergic child [6], while the first reported case series of buckwheat allergic patients was published by Rowe AH in 1937: the Author provided the first estimate of the prevalence of sensitization to buckwheat in USA (about 5.4% of sensitized patients among 500 subjects) [7]. About thirty years later, Horesh published another case series of 35 buckwheat allergic American children, and stated that exposure to buckwheat might have to increase in subsequent years, as buckwheat was increasingly used as food [8].

Apart from these early American studies, buckwheat allergy has been extensively studied in Asia where the crop is widely consumed. Noteworthy are the two studies published by Nakamura and Yamaguchi [9,10] in which they described 169 Japanese cases of buckwheat allergy recruited through a national survey sent to all university departments of internal medicine, pediatrics, dermatology and otolaryngology.

Epidemiology of Buckwheat Sensitization and Allergy

The population study of Takahashi et al. [11], published in 1998, is still the widest epidemiological study on buckwheat allergy ever published: they identified 194 buckwheat allergic children out of a population of 92680 subjects (estimated prevalence of buckwheat allergy: 0.22%), with symptoms ranging from urticaria (about 37.3% of allergic children) to wheezing (26.5%) and anaphylaxis (3.9%).

This study is, as far as we know, the first epidemiological survey on buckwheat allergy and it was also the only one, until our very recent publication on prevalence of buckwheat sensitization and allergy in Italy: the so called "I-SOBA" study [12]. This study, which included about 2000 pediatric and adult patients, showed a surprisingly high prevalence of buckwheat allergy in Italy: about 3.6% of subjects attending 18 allergy clinics. Prevalence of buckwheat sensitization was significantly higher in Northern regions of Italy where it is more used in the preparation of traditional dishes. However, many of the allergic reactions were elicited by buckwheat as hidden allergen in dishes that were not supposed to contain it (therefore acting as "hidden allergen"), and also these unexpected allergic reactions occurred more frequently in Northern Italian regions. The prevalence of buckwheat anaphylaxis seems to be of certain relevance in Asia (3.4% of all food anaphylaxis according to a Japanese survey on patients with food allergy [13] and

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Received March 03, 2014; **Accepted** March 28, 2014; **Published** April 02, 2014

Citation: Heffler E, Pizzimenti S, Badiu I, Guida G, Rolla G (2014) Buckwheat Allergy: An Emerging Clinical Problem in Europe. J Allergy Ther 5: 168. doi:10.4172/2155-6121.1000168

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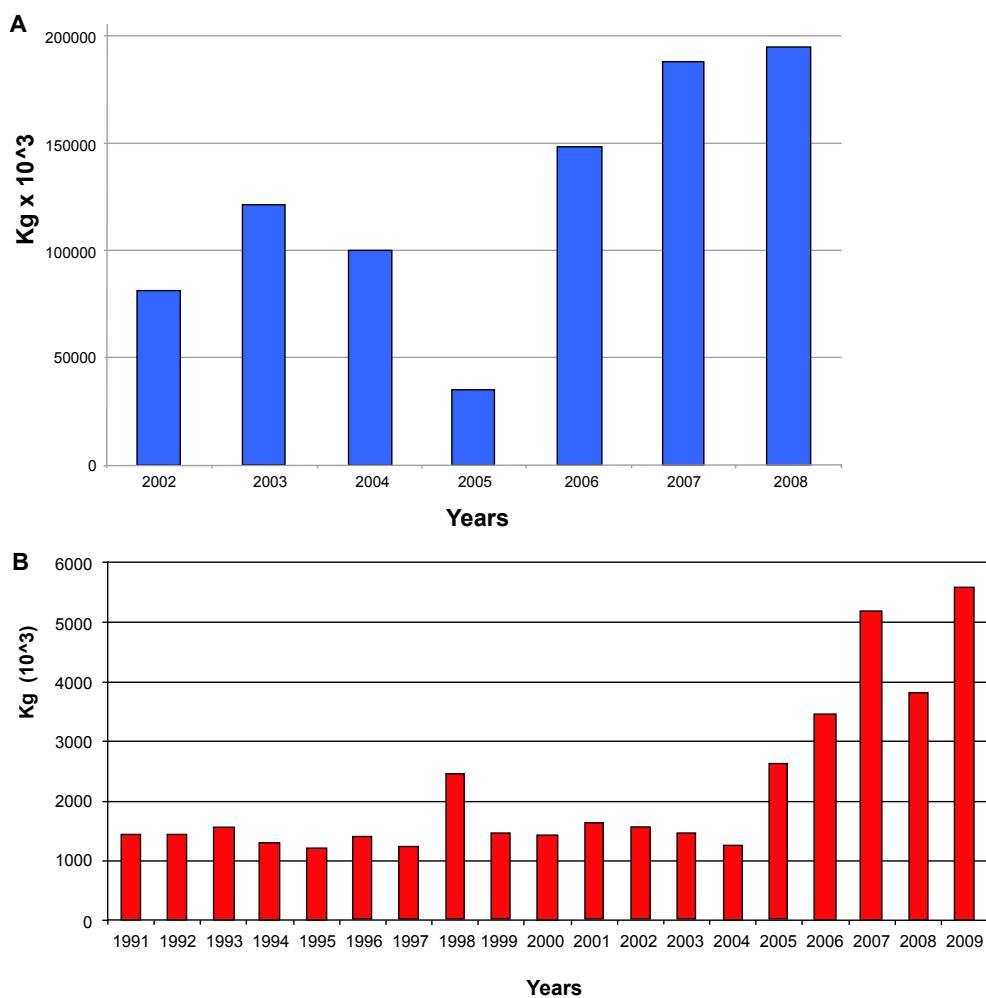


Figure 1: Net import of buckwheat in Europe (panel A-data from European Commission, Market Access Database: <http://madb.europa.eu/madb/indexPubli.htm>) and Italy (Panel B -data obtained by ISTAT, the Italian National Institute for Statistics: <http://www.coeweb.istat.it>).

2.9% according to a Korean retrospective study on patients reporting anaphylaxis [14]), while it is still unknown the prevalence of buckwheat anaphylaxis in Europe. A French study which analysed all the food anaphylaxis cases reported to the “French Allergy Vigilance Network”, showed that about 4.5% of them were due to buckwheat allergy [15], while an Italian epidemiological survey on food anaphylaxis reported a prevalence of about 1% of buckwheat anaphylaxis [16]. We showed that buckwheat allergy may explain about 7% of all the confirmed diagnosis of food allergies in Italy [2]. According to a more recent Italian survey [12] the prevalence of buckwheat sensitization is estimated 3.6% in patients referred to allergy clinics regardless of food allergy. As the consumption of buckwheat in Europe dramatically increased in the last few years, it is likely that the prevalence of buckwheat allergy, including buckwheat anaphylaxis, will increase in the next few years.

Review of Reported Cases of Food Allergy due to Buckwheat

Most of the reported cases of buckwheat allergy are single cases or at most small case series, which are from Asia or Europe.

Case reports of allergy to buckwheat were described after ingestion of “soba” noodles [17], French “galettes” [18], pasta [19,20], muesli

bars [21,22], Dutch “poffertjes” [23], crackers [24], cakes [25], pizza [1], bread [20,22], porridge [26] and a sweet buckwheat-cream [27]. Most of the described case reports are about anaphylaxis due to buckwheat allergy [17,18,21-26], and some of them are noteworthy for their particular clinical features: 1) a case of fatal buckwheat-dependent exercise-induced anaphylaxis in a 8-year old female child elicited by the ingestion of “soba” noodles few minutes before swimming [17]; 2) a case of buckwheat-induced anaphylaxis in a nurse sensitized to latex, one of the few known cross-reactive allergenic source for buckwheat [21]; 3) two cases of food allergy due to buckwheat ingestion in patients who probably got sensitized through the inhalation and/or the contact of buckwheat proteins contained into buckwheat-filled pillows [23,24].

Other IgE mediated reactions to buckwheat have been reported in cases of urticarial/angioedema [2,5], atopic dermatitis [27] and interstitial cystitis [28]. A peculiar case of food allergy to buckwheat, which was non-IgE mediated, was reported by Agata et al. [3]: the case of a 8 year-old child with pulmonary hemosiderosis (Heiner’s syndrome) due to hypersensitivity to buckwheat after the ingestion of noodles [5].

Buckwheat Allergens and known Cross-Reactivities

The protein content of buckwheat flour ranges from 6.5 to 33% of

the total weight depending on the cultivars and on the climatic and environmental conditions [29]. The most represented proteins are the so called “storage proteins” and in particular 13S globulins [30].

Several buckwheat proteins are described as being able to bind IgE in allergic patients, and proteins with molecular weight of 9, 16, 19, and 24 kDa are considered major allergens [31-35] (Table 1). It has recently been suggested that sensitization to specific buckwheat allergens would be related to specific symptoms, leading to three different clinical patterns. Predominant gastrointestinal symptoms are more commonly observed in patients sensitized to a 16-kDa protein, who show grass and wheat flour co-sensitization; predominant cutaneous symptoms are more commonly observed in patients sensitized to a 25-kDa protein, who are rarely co-sensitized to other allergens; and anaphylaxis, which is more commonly observed in patients sensitized to a 40-kDa protein, who also are rarely co-sensitized to other allergens [2].

Clinically relevant cross-reactivity between buckwheat proteins and other allergens have been described for latex (*Hevea brasiliensis*) [21,36], rice [37], poppy seeds [38,39] and hazelnuts [39].

Buckwheat as a “Hidden Allergen”

In at least three case reports, buckwheat was the causative allergen in dishes which were not supposed to contain it, therefore acting as a “hidden allergen”. In 1995, Wüthrich and Trojan [40] described a case of anaphylaxis after ingestion of a vegetarian “wheat-burger” which was contaminated by buckwheat; in 2001 Yuge et al. [41] published a case report of a patient who experienced anaphylaxis due to buckwheat contained into a pepper compound; more recently, we described the case of a patient who had several episodes of anaphylaxis after eating pizza in some restaurants, but well tolerating the same dish served in other restaurants: the causative allergen was buckwheat contained into a mix of flours used to prepare pizza dough in some restaurants [1].

In a study we published in 2011 on 24 confirmed cases of buckwheat allergy, the great majority (about 87.5%) of patients experienced their allergic reactions after ingestion of buckwheat as “hidden allergen” (2); similar results were obtained in a recently published epidemiological survey on buckwheat sensitization, in which two thirds of the described allergic reaction were due to hidden buckwheat in dishes like pizza or cakes [12].

Discussion

Buck wheat allergy is well known and frequent in Asia, where buckwheat is a common food, since long time ago [9-11]. In Europe and USA, buckwheat allergy was an anecdotal description since the last few years, when the interest on this allergenic source increased due to reports of relevant prevalence of buckwheat allergy outside Asia [2,12]. This high prevalence of buckwheat allergy in some European countries has been related to the increased consumption of this crop due to several reasons: the tendency to use it into mixes of flours to

Name of the allergen	Family	Biological function	Molecular weight	Other isoforms
Fag e 1	13S Globulin	Legumin-like protein	24 kDa	Fag e 1.0101
Fag e 2	2S Albumin	2S Albumin	16 kDa	Fag e 2.0101
Fag e 3	7S Vicilin	7S Vicilin-like globulin	19 kDa	Fag e 3.0101
Fag e 10kD	Alpha-amylase/Trypsin inhibitor	Alpha-amylase/Trypsin inhibitor	10 kDa	
Fag e T1	Trypsin inhibitor	Trypsin inhibitor	7 kDa	

Table 1: Main buckwheat allergens and their characteristics.

prepare pizza or bread [1,2], the increased diffusion of the so-called “minor cereals” through the network of “organic food shops”, and the increased diffusion of ethnic diet.

Buckwheat is increasingly used in the gourmet and ‘free- from’ food sectors, particularly in gluten free foods, which are not only consumed by coeliac patients, but by thousands of people without a gluten intolerance or allergy. According to the Food Standards Agency [42], the British gluten-free market is worth £238 million annually and grew by more than 15 per cent last year. In the US, it’s worth around \$2.6 billion, a growth of 36 per cent since 2006, with predictions it may double in size in the next two years [43].

A particular aspect of allergic reactions to buckwheat reported in Europe is that they are often severe and systemic, such as anaphylaxis [17,18,21-26], and often triggered by buckwheat undeclared (“hidden”) in dishes which are not supposed to contain it like pizza dough, wheat burgers, pasta, multicereal bread and pepper [1,2,12,40,41].

Conclusion

Buckwheat allergy merits awareness in the Europe since exposures are likely to increase via a more ethnically diverse diet plus increasing use of buckwheat in popular food sectors. Failure to recognise buckwheat allergy could expose individuals to considerable risk.

We recommend that clinicians suspect and test for buckwheat allergy when evaluating patients with symptoms suggestive of food allergy, when the reaction follows the ingestion of dishes possibly made by mix of flours (where buckwheat can be a “hidden allergen”), and we hope that health authorities will consider including buckwheat in the list of allergens to be declared in food products.

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This article was originally published in a special issue, **Food Allergy handled** by Editor. Dr. Glover Sarah Camille, University of Florida, USA.