

Food Anaphylaxis: Reported Cases in Russian Federation Children

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Abstract Background: Anaphylaxis is a potentially fatal allergic reaction. Food allergy is one of the main causes of anaphylaxis in children. Anaphylaxis research in different populations across Europe is one of the unmet needs. The aim of this study is to evaluate typical clinical features, causes of food anaphylaxis and sensitization to food allergens in Russian Federation children admitted to the allergy department. **Materials and methods:** Allergy history of 80 children with food anaphylaxis was investigated and specific IgE concentration in serum was tested.

Results: Total number of anaphylaxis episodes in 80 children was 158. Family allergy history was positive in 42 children. Food anaphylaxis episodes were associated more often with cow milk, fish or/and seafood, tree nuts. Cow milk was reliably more valid in children under 2 years of age than in older children, where tree nut and fruit anaphylaxis was more frequent. Specific IgE levels $\geq 0,35$ kUA/l to food associated with anaphylaxis episodes were revealed in all children and varied largely. Specific IgE levels did not correlate with severity of anaphylaxis episodes. Clinical manifestations with skin/mucosa and respiratory system involvement were the most frequent (97,5% and 92% respectively). Cardiovascular and gastrointestinal systems were involved in 33,5% of cases each. **Conclusion:** Cow milk, fish and/or seafood, tree nuts are the most often food associated with food anaphylaxis cases in Russian Federation children. Food triggers of anaphylaxis vary with age of children. Skin/mucosa and respiratory tract are often involved in food anaphylaxis episodes. Cardiovascular involvement increases with children's age.

Keywords: anaphylaxis, children, infants, food

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1. Introduction

A widely used definition of anaphylaxis is "a serious allergic reaction that is rapid in onset and may cause death" [1]. 1 in 300 of the European population is affected by anaphylaxis at some time in his life [2]. Food allergy may be the cause of anaphylaxis in up to 50% in general population [3]. Food anaphylaxis prevalence is estimated as 0,5-16/100,000 person-years [3,4,5].

In children's population food allergy is one of the main cause of anaphylaxis. Up to 81% cases are due to food allergy [6,7,8].

Any food product may result in anaphylaxis. Despite the huge range of consumed food, the main food allergens in adults as well as in children are: peanut, tree nuts (cashew, Brazil nut, walnut, black nut, filbert), milk, hen's egg, fish and seafood [1,3,9]. The importance of food allergens in anaphylaxis varies upon the age of a patient, physical and chemical properties of foodstuff proteins and their allergenicity.

Since many important aspects of food allergy and anaphylaxis are not sufficiently understood, anaphylaxis

and food allergy research are prioritized by Horizon 2020 and the EU's third public health program. EAACI Research Needs in Allergy Position Paper [10] points out the essential and urgent unmet needs for research of anaphylaxis in different populations across Europe.

Anaphylaxis has not been studied well in Russia and this study is one of the first attempts to. The aim of this study is to evaluate typical clinical features, causes of food anaphylaxis and sensitization to food allergens in Russian Federation children admitted to the research center allergy department.

2. Materials and Methods

Research and Clinical Institute for Pediatrics is a large state pediatric center of Russian Federation. The study has been approved by the medical Ethics Committee of the Research and Clinical Institute for Pediatrics at the Pirogov Russian National Research Medical University (protocol №24/11) and meets the principle of Helsinki agreement declaration.

In a four-year period (from October 2011 to February 2015) 80 children were admitted to the Allergy and

Clinical Immunology Department with a history of food anaphylaxis. A written consent form was signed by all patients enrolled in this study, or by their parents. Clinical data associated with the allergy history and the reports were evaluated according to European Academy of Allergy and Clinical Immunology diagnostic criteria of anaphylaxis [11].

An allergy survey was performed in all children. Specific IgE concentration in serum was tested with a fluoro-immunoassay (ImmunoCAP 100, Phadia AB, Sweden). The immunoassay was performed eight or more weeks after the previous anaphylaxis episode. Spectrum of allergens tested was determined in every patient individually, considering his history of anaphylaxis. IgE level 0,35 κ UA/l or more was supposed positive; 100 κ UA/l or more was read as 100 κ UA/l.

Median, upper and lower quartiles were calculated. Nonparametric Fisher's test was used to define the difference in two groups tested. Correlation of IgE levels with severity of anaphylaxis episodes was analyzed with Spearman rank correlation test. The level of statistical significance was set at $p < 0.05$. Statistical analysis was performed with STATISTICA 8.0.

3. Results

30 girls (37,5%) and 50 boys (62,5%) were enrolled in the study. Age of children varied from 8 months to 18 years with median at 6 years ([Q1 3years; Q3 10 years]).

Family allergy history was positive in 42 children with paternal relatives involved in 21 children (50%), maternal in 17 (40,5%), both paternal and maternal relatives involved in 4 (9,5%) children. Fathers of two children with anaphylaxis to seafood and nuts reported about their anaphylaxis to the same food allergens.

Other allergic diseases were reported in 75 (93,7%) children. Atopic dermatitis was diagnosed in 57 of 75 children (76%), allergic rhinitis in 40 (53,3%), asthma in 39 (52%), urticaria in 18 (24%), angioedema in 9 (12%) children.

Food anaphylaxis to more than one allergen (up to different 5 allergens) was in 28 children (35%). Anaphylaxis to one allergen (i.e. cow milk containing food products) repeated during lifetime was in 33 (41%) children.

Single episode of anaphylaxis was diagnosed in 30 (40%) children, more than one episode in 50 (60%) children.

Total number of anaphylaxis episodes in 80 children was 158, in which 140 cases (88,6%) happened at home, 13 – at public catering places, 5 – at the kindergarten.

3.1. Food Associated with Anaphylaxis Episodes

Food anaphylaxis was associated more often with cow milk (40%), fish or/and seafood (33%), tree nuts (24%) (Table 1).

Table 1. Food associated with anaphylaxis and a number of anaphylaxis episodes per food allergens

Food	Number of positive children	% of positive children (n=80)	Number of anaphylaxis episodes	% of anaphylaxis episodes (n=158)
Cow milk	33	41,2%	49	31%
Fish or/and seafood	27	33,7%	33	20,9%
Tree nuts	18	22,5%	21	13,3%
Fruits	16	20%	18	11,4%
Hen's egg	15	18,7%	17	10,7%
Peanut or/and bean	7	8,7%	10	6,3%
Goat milk	3	3,7%	3	1,9%
Wheat	2	2,5%	2	1,3%
Buckwheat	2	2,5%	2	1,3%
Chicken meat	2	2,5%	2	1,3%
Rabbit meat	1	1,2%	1	0,6%

Food associated with first anaphylaxis episode, considered to differ during lifetime because of feeding aspects and diet early in life. To analyze this, a total number of children were divided into two groups in accordance with age of first anaphylaxis reaction. First

group (n = 46) - infants under 2 years of life with age Me = 0,7 years [Q1 0,5 year; Q3 1 year]. Second group (n = 34) - children older than 2 years with age Me = 4 years [Q1 2 years; Q3 7 years] (Table 2).

Table 2. Food associated with first anaphylaxis episode in children under and over 2 years of age

Food	All children (N=80)		Infants < 2 years (n=46)		Children 2-18 years (n=34)	
	Absolute number	%	Absolute number	%	Absolute number	%
Cow milk	28	35	26 *	56,5	2 *	5,9
Fish or/and seafood	15	18,7	6	13,1	9	26,5
Tree nuts	10	12,5	0 †	0	10 †	29,4
Hen's egg	9	11,3	7	15,2	2	5,9
Peanut or/and beans	4	5	1	2,2	3	8,8
Fruits	11	13,8	3 ‡	6,5	8 ‡	23,5
Goat milk	3	3,7	3	6,5	0	0

* and † $p < 0,0001$; ‡ $p < 0,05$.

Cow milk, fish or/and seafood, fruits were the most frequent food associated with first anaphylaxis episode in infants (35%, 18,7% and 13,8% respectively).

Reliable difference was revealed in cow milk anaphylaxis, which was more frequent in infants under 2 years of age than in children at the age 2 years and older.

Tree nut anaphylaxis and fruit anaphylaxis were more frequent in children over 2 years of age than in infants.

The way of contact with food was analyzed. All children had anaphylaxis episodes after food ingestion. Later on, keeping strict diet recommendations, 8 children had anaphylaxis episodes after skin contact with food (milk, hen's egg, fish or/and seafood); 10 children - after inhalation contact with fish or/and seafood during thermal cooking process.

3.2. Allergy Survey

Allergy tests were positive (sIgE $\geq 0,35$ κ UA/l) to food associated with anaphylaxis episodes in all children (n = 80). There was a wide range of specific IgE levels revealed (Figure 1). Specific IgE levels did not correlated with severity of anaphylaxis episodes ($p > 0,05$, Spearman rank correlation test).

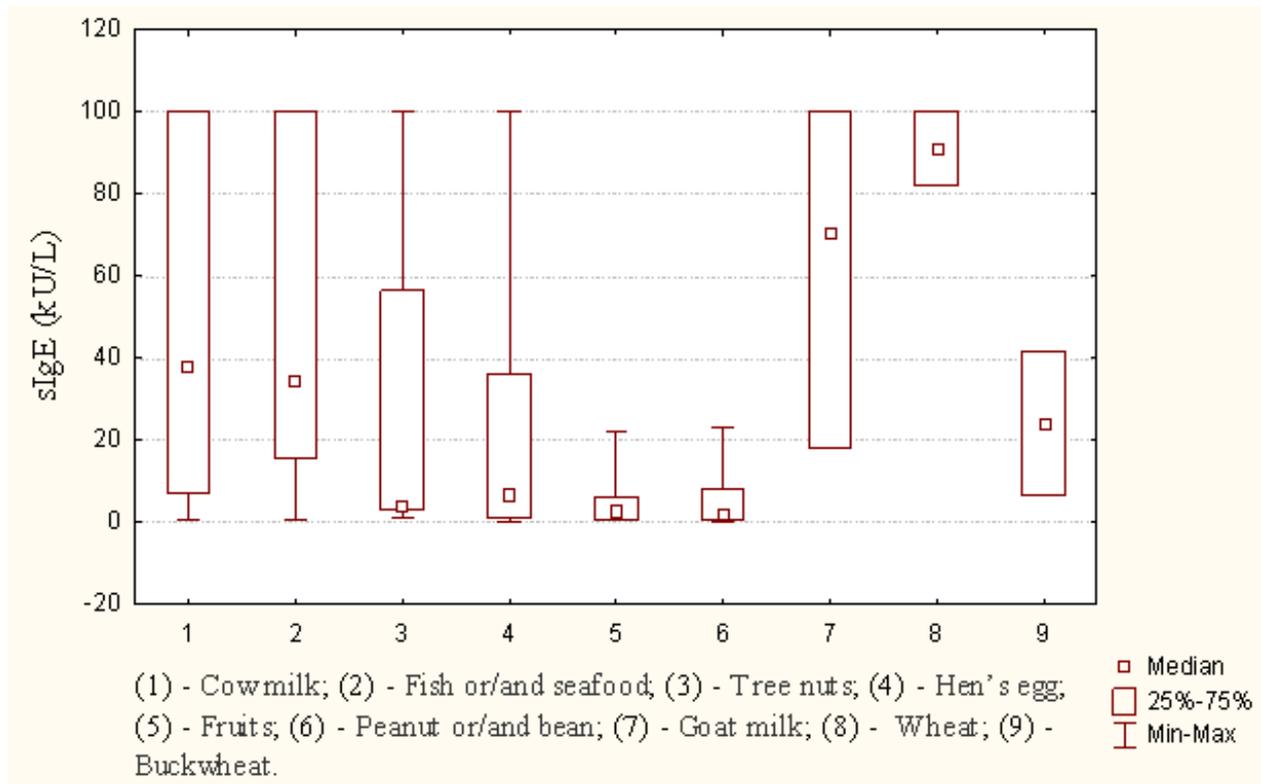


Figure 1. Specific IgE levels to food allergens in serum of children with food anaphylaxis

It should be noted that in children with fish anaphylaxis and sIgE level ≥ 100 κ UA/l (n=11), anaphylaxis episodes due to inhalation contact were in 54,5% of cases. In patients with fish anaphylaxis and sIgE < 100 κ UA/l (n=16), anaphylaxis episodes due to inhalation contact was twice less often (25% of cases). Nevertheless reliable distinctions in the frequency were not revealed ($p > 0,05$).

Table 3. Clinical manifestations frequency in food anaphylaxis episodes in children

System involved	Clinical signs	(% of n)
Skin/mucosa (n=154)	Urticaria	70%
	Angioedema	75%
	Itch	60%
Respiratory tract (n=146)	Wheeze	73%
	Cough	87%
	Chest tightness	20%
	Nose congestion/sneezing	43%
Central nervous system (n=71)	Drowsiness	85%
	Dizziness	18%
	Loss of consciousness	12%
Gastrointestinal tract (n=53)	Vomiting	78%
	Diarrhea	27%
	Abdominal pain	23%
Cardiovascular system (n=53)	Tachycardia/bradycardia	28%
	Hypotension	60%

3.3. Clinical Manifestation

Clinical manifestations covered various organ systems (Table 3). Skin/mucosa and respiratory system involvement were the most frequent (97,5% and 92% respectively). Central nervous system involvement was less often (45%). Cardiovascular and gastrointestinal systems were involved in 33,5% of cases each. There were no lethal cases of food anaphylaxis registered in the study.

4. Discussion

This survey is first in Russian Federation children to approach food anaphylaxis triggers and clinical manifestations.

Parents' allergy is recognized to be a risk factor for atopy in children [12,13,14]. We revealed a positive family history in a half of the enrolled patients. Food anaphylaxis was single only in 5 children; all other patients had allergic diseases as well. The same results are published by Novembre E et al. 1998 [15] and de Silva IL et al. 2008 [16].

Clinical manifestations of food anaphylaxis were taken place at home in most of the patients (88,6%) and triggered by a wide range of food. Cow milk was the most

frequent trigger in Russian Federation children (31% of cases). This food is reported to be the major trigger in Portugal (52%) and Iran (47%) food anaphylaxis surveys [17,18]. In other countries food anaphylaxis triggers are reported different. Peanut and seafood are on the first place in the USA [15,19,20]; peanut and tree nuts – in Australia, Germany, Italy and Turkey [3,16,21,22]; seafood and hen's egg – in Asia [23,24].

Polyvalent food anaphylaxis was registered in our research in 35% of children. More than 1/3 of children had repeat of anaphylaxis to the same food product. Such a large amount of repeated cases is supposed to be in connection with a lack of information in parents on life-threatening nature of anaphylaxis, poor knowledge on food products allergen composition and insufficient elimination of allergen traces in households. Elimination of food was not strict in many families, which results in difficulties of food anaphylaxis prevention.

Surveys considering the age of children report cow milk and hen's egg as main triggers of food anaphylaxis in young children; fish, seafood, tree nuts, peanut and fruits in older children and adults [19,20]. Similar associations were demonstrated in our research. Food anaphylaxis after cow milk ingestion was nearly ten times more frequent for the first two years of life in infants compared to children older than two years. Manifestations of food anaphylaxis after tree nuts and fruits ingestion are more frequent in children over two years of age.

IgE-mediated allergic reactions are declared to be a mechanism of food anaphylaxis [4]. IgE profile in Russian Federation food anaphylaxis children revealed sensitization in all examined children. This feature is in agreement with Saeideh B survey [18], but there are specific differences. Sensitization in Russian Federation children was variable and did not correlate with anaphylaxis severity. Sensitization was related to a certain degree with inhalation hypersensitivity to fish and/or seafood for anaphylaxis.

Clinical manifestations of food anaphylaxis in Russian Federation children involved skin/mucosa and respiratory tract most often. The same frequency prevalence was reported by other authors [5,15,16,20]. Cardiovascular system involvement was reliably more often in Russian Federation children over two years of age. The increase of cardiovascular symptoms frequency with age was reported throughout childhood and in adults compared with children [16,24,25].

The limitation of the study may be defined by the suggestion that a certain number of food anaphylaxis cases registered in our study could be idiopathic with food sensitization related to other allergy diseases. Nevertheless, the proper diagnostic criteria of anaphylaxis used with clinical history of episodes give us confidence in clear realization of food anaphylaxis diagnosis.

5. Conclusion

Food anaphylaxis in Russian Federation children is in a research focus of local allergists. Cow milk, fish and/or seafood, tree nuts are most often associated with food anaphylaxis cases. First episode of food anaphylaxis is associated with milk products in a large amount of cases. Food triggers of anaphylaxis vary with age of children.

Skin/mucosa and respiratory tract symptoms are often involved in food anaphylaxis episodes. Cardiovascular involvement increases with children's age. There are certain difficulties in repeat cases prevention, since a lack of information in parents on life-threatening nature of anaphylaxis, poor knowledge on food products allergen composition, polyvalent food anaphylaxis and insufficient elimination of allergen traces in households of the Russian Federation.

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