Peanut induced anaphylaxis in children and adolescents: data from the European Anaphylaxis Registry

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Abstract

Background: Peanut allergy has a rising prevalence in high-income countries, affecting 0.5–1.4% of children. This study aimed to better understand peanut anaphylaxis in comparison to anaphylaxis to other food triggers in European children and adolescents. Methods: Data was sourced from the European Anaphylaxis Registry via an online questionnaire, after in-depth review of food induced anaphylaxis cases in a tertiary paediatric allergy centre. Results: 3514 cases of food anaphylaxis were reported between July 2007 - March 2018, 56% in patients younger than 18 years. Peanut anaphylaxis was recorded in 459 children and adolescents (85% of all peanut anaphylaxis cases). Previous reactions (42% vs 38%; p=0.001), asthma comorbidity (47% vs 35%; p<0.001), relevant co-factors (29% vs 22%; p=0.004) and biphasic reactions (10% vs 4%; p=0.001) were more commonly reported in peanut anaphylaxis. Most cases were labelled as severe anaphylaxis (Ring&Messmer grade III 65% vs 56% and grade IV 1.1% vs 0.9%; p=0.001). Self-administration of intramuscular adrenaline was low (17% vs 15%), professional adrenaline administration was higher in non-peanut food anaphylaxis (34% vs 26%; p=0.003). Hospitalisation was higher for peanut anaphylaxis (67% vs 54%; p=0.004). Conclusions: The European Anaphylaxis Registry data confirmed peanut as one of the major causes of severe, potentially life-threatening allergic reactions in European children, with some characteristic features e.g. presence of asthma comorbidity and increased rate of biphasic reactions. Usage of intramuscular adrenaline as first line treatment is low and needs to be improved. The Registry, designed as the largest database on anaphylaxis, allows continuous assessment of this condition.

Introduction

The population-level burden of childhood food allergy (FA) is increasing, with growing epidemic and severity of reactions. Over the last decade several review articles have reported a significant increase in food induced anaphylaxis related Emergency Department visits in children (1)(2).

Peanut is one of the major food allergens in children, with increasing prevalence. In the United States, the prevalence of peanut allergy more than tripled between 1997 and 2008, with a recent study finding another 21% increase since 2010 (3). In the UK, reported rates of peanut allergy in 3- to 5-year-old children increased from 0.5% in 1989, to 1.2% in 2001–2002 in the same geographical area (4).

Peanut allergy affects 1.4-4.5% of children and nearly 50% of peanut allergic individuals have had a past severe reaction (5). The European Anaphylaxis Registry reports peanut as an elicitor for anaphylaxis from infancy to young adulthood, triggering nearly one third of food induced anaphylaxis in the paediatric cohort (6).

Reactions are unpredictable in relation to occurrence, severity and outcome and occur despite the appropriate allergen avoidance. Uncertainty results in a perception of risk that adversely affects health-related quality of life (HRQoL) (7). Also absence of evidence regarding reliable severity predictor markers contributes to patient's and parents' lack of control over their environment with further consequences on HRQoL.

This study aimed to provide a comparison between anaphylaxis to peanut and other food triggers in European children and adolescents, with regards to atopic history, previous reactions, co-factors, symptoms timing and severity, emergency and long-term management.

Material and Methods

Data Source

Data was sourced from the European Anaphylaxis Registry, a database that collects data regarding anaphylactic reactions from 137 specialized tertiary allergy centres in ten European countries (Germany, Austria, Switzerland, Poland, Italy, Spain, Ireland, Greece, France, Bulgaria), and Brazil. Data collection is based on an online questionnaire which continuously developed over time to include additional information, mainly focused on elicitor(s), symptoms, course of reaction, co-factors, emergency treatment, diagnostic procedures and preventive/long-term management (current version 8.0).

Pseudo-anonymized data of patients with anaphylaxis were reported, after in-depth review of the anaphylaxis cases by trained health care professionals from a tertiary allergy centre. On their first visit in the centre

parents were asked to provide written informed consent to allow registration of the child's medical history and reaction details in the database after completion of the diagnostic workup.

Ethical approval was obtained from the Ethics Committee, Charité - Universitätsmedizin Berlin, Germany (the coordinating centre), as well as from the local Ethic Committees in all participating centres.

Study Group

The study cohort included patients younger than 18 years, reported between July 2007 and March 2018, with moderate and severe anaphylaxis triggered by food (Figure 1). For comparison analysis was performed on the peanut anaphylaxis subgroup versus the subgroup of anaphylaxis triggered by other food.

Only cases fulfilling the modified National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network (NIAID/FAAN) diagnostic criteria for anaphylaxis were included. The severity of reaction was graded according to the Ring&Messmer classification (grade II-IV). Peanut as an elicitor was ascertained by the local allergy specialist based on in-depth diagnosis.

Variables

The study analysed data regarding atopic history, previous reactions, co-factors, symptoms, severity and timing of reaction, emergency treatment and long-term management. Variables were reported as a fraction of valid answer options, with multiple selections possible for some questions. All variables except for age at reaction, gender and symptoms were allowed to remain missing by item, therefore the denominator used to calculate percentages did slightly vary from the total for some variables. Specific areas covered and the online version can be accessed through www.anaphylaxie.net.

Statistics

Statistical analysis was performed using IBM SPSS Statistics 25 (Chicago, IL, USA).

Basic frequency distributions were used to describe different characteristics: demographic data, atopic history, co-factors, symptoms, severity and timing of reactions, pre-hospital and medically administered care, long-term management. Mann-Whitney U test was used for comparison between the 2 subgroups; a p value <0.05 was considered to be statistically significant.

Results

3514 cases of food anaphylaxis were reported between July 2007 and March 2018, 56% in patients younger than 18 years (n=1962). Anaphylaxis due to peanut was recorded in 459 children and adolescents, representing 85% of all registered cases of peanut anaphylaxis (n=541; 15% of all food triggered anaphylaxis). Other food caused anaphylaxis in 1503 cases (51% of all non-peanut food anaphylaxis), with cow's milk, hen's egg, hazelnut and cashew as lead elicitors.

Median age of affected patients was higher in the peanut subgroup compared to the other food cohort (5 years, range 8 months to 17 years vs 4 years, range 1 month to 17 years; p<0.001), with a slight predominance in boys in both subgroups (F:M ratio of 1:1.5 and 1:1.8 respectively). More than half of the peanut cohort were pre-schoolers aged 0-6 years (n=282; 61%), followed by children 7-12 years (n=115; 25%) and adolescents 13-17 years (n=62; 14%), which was comparable to the other food cohort (65%, 20%, 15%) (Table 1).

The countries with the most frequent reports of peanut induced anaphylaxis in children/adolescents compared to the total case reports aged <18 years were France (n=92; 23%), Germany (n=242; 18%), Ireland (n=28; 17%), Switzerland (n=65; 15%) and Austria (n=13; 14%). Less than 10 cases of peanut anaphylaxis were reported from Greece, Spain, and Brazil, but also from Poland and Bulgaria. No case of peanut induced anaphylaxis was registered in Italy (Figure 2).

History and cofactors

History of at least one previous reaction to peanut, usually milder, was more common (n=192; 42%) than the same history in the other food anaphylaxis subgroup (n=569; 38%) (p=0.001). Previous anaphylaxis to

peanut was reported in 23 cases (12%), and to other food in 88 cases (15%) (Table 1).

Peanut allergy was already diagnosed before the recorded anaphylaxis in 45% of cases (n=167, specified in n=371 out of 459), significantly higher than for other food triggers (33%; n=409, specified in 1243 out of 1503) (p<0.001) (Table 1).

Allergic comorbidities were frequent in both subgroups (n=296; 64% vs n=991; 66%). Asthma was more common in the peanut cohort (n=150; 47% vs n=359; 35%; p<0.001), with no difference in the frequency of respiratory symptoms between children with or without concomitant asthma (data not shown). Eczema was more frequent in the other food triggers subgroup (n=126; 40% vs n=525; 51%; p=0.035), and there was no statistically significant difference between the two subgroups regarding frequency of allergic rhinitis (36% vs 33%), and other food allergy (27% vs 32%) (Table 1).

Relevant cofactors, potentially influencing allergenic threshold, were more commonly reported in peanut anaphylaxis (n=114; 29%) compared to other food triggers (n=281; 22%) (p=0.004). Physical exercise (80% vs 77%; p=0.002) and infection (14% vs 13%) were the most frequent co-factors (Table 1).

Location

There was no statistically significant difference in terms of location for peanut or other food induced anaphylaxis. Most events happened in the country of residence (97% vs 98%) predominantly at home (42% vs 50%), in school or kindergarten (12% vs 9%), and in a relative's or friend's house (11% vs 7%).

Non-prepacked products were responsible for only 38% (n=123) of the peanut reactions (specified in n=320 out of 459), compared to other foods, where they triggered the majority of the events (63%; n=610 out of 972 cases with this information available) (p=0.005) (Table 1). Milk and egg (63%; p<0.001), but also some tree nuts (53%; p<0.001) were main ingredients in non-prepacked food. Products were catered or bought (e.g. bakery, supermarket). Peanut was more often listed as an ingredient or on precautionary allergen labelling compared to other food allergens (54% vs 40%; p=0.001), but 45% (n=120) and 58% (n=386) respectively answered 'don't know' to this question.

Small amounts (less or equal to 1 teaspoon) were more likely to elicit the reaction in peanut anaphylaxis (66%; n=197 specified in n=300 out of 459 vs 43%; n=446 specified in n=1034 out of 1503; p<0.001) (Figure 3).

Symptoms, severity and timing of reaction

Respiratory (92% vs 90%) and skin (91% vs 94%; p=0.009) were the organ systems most frequently affected in both subgroups. Gastro-intestinal symptoms were more common in peanut anaphylaxis (59% vs 50%; p=0.003) and there was no statistically significant difference for cardio-vascular involvement between subgroups (36% vs 35%).

According to the Ring&Messmer classification the majority of cases in both subgroups were labelled as severe anaphylaxis, however significantly more in the peanut cohort: grade III (65% vs 56%; p=0.001) and grade IV (1.1% vs 0.9%) (Table 1).

Death was recorded in 0.7% (n=3) in the peanut cohort, and in 0.3% (n=5) in the other food cohort. The 3 cases of fatal peanut anaphylaxis occurred in 2006, 2012 and 2013. They were all female teenagers, two of them had other food allergies/atopic disease, and stress was given as possible cofactor in one case. First line treatment was unknown in one case and provided by an emergency professional in the other two, but only one received adrenaline (i.m. and i.v.) as well as oxygen and i.v. fluid volume. Other confirmed food triggers causing fatal anaphylaxis were cow's milk (2 cases), snail, and poppy seeds, whereas kiwi or hazelnut were suspected in another case.

Analysis of the interval between exposure and onset of symptoms revealed no differences between peanut and other food triggered anaphylaxis: 49% (n=226; specified for 366 out of 459 cases) and 48% (n=714; specified for 1219 out of 1503) respectively reacted within 10 minutes after exposure to the trigger, and another 18%

(n=83) and 21% respectively (n=310) within 30 minutes. In both subgroups 6% of the patients reported a delayed reaction with an

interval of more than 1 hour.

The frequency of biphasic reactions was significantly higher for peanut anaphylaxis compared to other food triggers (10%, specified for n=404 out of 459, vs 4%, specified for n=1314 out of 1503; p=0.001) (Table 1). The second reaction occurred after more than 12 hours in 21% of the cases in both subgroups. For peanut anaphylaxis, there were no statistically significant differences between the biphasic and non-biphasic reactions in terms of age, reaction severity, and administration of adrenaline.

Emergency treatment

First-line treatment was administered in 89% of peanut anaphylaxis and 91% of reactions triggered by other food.

24% of cases in the peanut subgroup and 27% in the other food subgroup were solely lay treated, mainly by a family member (80% vs 81%). Another 12% and 13% respectively were initially cared for by a lay person followed by a professional. 17% (n=28) of the peanut allergic children self-administered an adrenaline auto-injector (AAI), with a similar figure (n=78; 15%) for other food triggers. Lay treatment also included oral antihistamines (63% vs 79%; p<0.001), oral steroids (46% vs 50%) and beta2-agonist inhalers (35% vs 25%; p=0.008) (Table 2).

Emergency treatment was carried out solely by a healthcare professional in 52% of the peanut subgroup and 61% of the other food subgroup. 39% vs 44% were treated by an emergency physician, and 14% vs 11% by a general practitioner. Professional treatment included adrenaline (intramuscular (i.m.), intravenous (i.v.), and inhalative) (26% vs 34%; p=0.003), antihistamines (i.v. and oral) (68% vs 66%), corticosteroids (i.v., oral, and rectal) (74% vs 70%), or beta2-agonist (i.v., oral, and inhalative) (31% vs 25%; p=0.044) (Table 2).

Almost one in two peanut allergic children (44%) already prescribed an AAI did not use or carry the device. The percentage was slightly higher but not statistically significant for other food allergies (53%) (Table 2).

Second-line treatment (i.e. additional doses or other drugs not used for initial management, with failure of first-line treatment) was reported in 24% of peanut allergic children (n=93 out of 388 cases with this information available), with no significant difference compared to the other food subgroup (19%; n=248 out of 1279 cases with this information available). A second dose of adrenaline was administered in 5% (n=10) of peanut anaphylaxis and 6% (n=41) in the non-peanut food group (Table 2).

Hospitalisation was required in a higher number for peanut anaphylaxis compared to other food (67% of 280 cases with known hospitalisation status vs 54% of 998 cases, p=0.004), but there was no difference regarding admission to Intensive Care Unit (6% vs 5%) (Table 2).

Tryptase testing was performed outside the episode in 21% of cases in both subgroups. Elevated serum levels were only registered in a small percentage and with no statistically significant difference between the 2 subgroups (14% vs 6%).

Long-term management plan

Almost all children received counselling about trigger avoidance (97% vs 95%). Emergency drugs prescription was significantly higher for peanut anaphylaxis (97% vs 93%; p=0.009), but training in an emergency plan was similar between the 2 subgroups (96% vs 94%).

AAIs were more prescribed for peanut anaphylaxis compared to other food (96% vs 89%; p=0.003), as well as inhaled beta2-agonists (45% vs 36%; p=0.002), with no difference for antihistamines (97% vs 96%) and corticosteroids (90% vs 87%) (Table 2).

Discussion

Food is the leading known cause of anaphylactic reactions for children and adolescents in emergency departments in the United States and Europe, with geographical variations according to local dietary habits and food exposures (8). Peanut is not only one of the most common food trigger, but also one of the commonest trigger in anaphylaxis fatalities in the UK and USA (7). The authors chose to provide a comparison between anaphylaxis to peanut and other food triggers, although the different foods included and analysed as a group represent different entities and considerably different diseases.

Within the European Anaphylaxis Registry, Western European countries reported the majority of peanut induced anaphylaxis cases, but the Registry doesn't collect data from all over Europe. There was no overlap between these countries and the ones with the highest reports of food triggered anaphylaxis, in particular Mediterranean countries like Greece, Spain and Italy with high frequency of food allergy but not peanut.

The findings of the European Anaphylaxis Registry support previously published findings from other multi (MIRABEL) (9)- or single (Riley)-centred registries (10) that peanut allergy is more common in pre-school aged boys. These data bases included children with peanut allergy and/or sensitisation not only cases of peanut induced anaphylaxis. Similar demographics with predominance of males in younger age groups was described in several food-induced anaphylaxis studies (11)(12)(13). The lower median age in the other food subgroup is likely explained by cow's milk and egg being the predominant elicitors of allergic reactions in children in the first two years of life.

Previous milder reactions were more frequent in peanut allergic children (42%) compared to other food triggers (38%), but there was no difference for previous anaphylaxis. Sicherer et al. (14) showed that almost 50% of children experience accidental exposure to peanut within 2 years of their first reaction, proving that avoidance is not enough. The Riley Registry (10) reported anaphylaxis with second exposures in 33.9% of children, and in 33.3% of children who had anaphylaxis with first exposure. On a larger scale (38.408 children) Gupta et al. (15) reports an estimated 42.3% of children with a food allergy to have a history of at least one severe reaction, and 42% to have at least one lifetime food allergy-related visit to the emergency department.

The majority of cases had a background of atopy, regardless of the eliciting food, with similar frequencies for atopic dermatitis, allergic rhinitis, asthma, and other food allergies/sensitisations to other studies (9). Eczema was more frequent in children allergic to foods other than peanut, likely in the younger group of infants and toddlers with cow's milk and/or egg allergy, in line with the natural history of this condition. Asthma was more common in the peanut anaphylaxis cohort. Leickly et al. (10) reports that children with peanut anaphylaxis were significantly more likely to have asthma ($P < .001$) and other food allergies ($P = .04$) than those with non-anaphylactic reactions to peanut.

The prevalence of co-factors in anaphylaxis is reported to be around 30% in adults (16) and 18% in children (17). Our data reports relevant co-factors more frequently in peanut anaphylaxis (29%) compared to other food triggers (22%), with physical exercise in the lead. Previous data from the Registry (17)(6) also reported physical exercise to be the most frequent co-factor, followed by medication. There is a lack of published data on other large children anaphylaxis cohorts for comparison.

Non-prepacked food products were only responsible for one out of three peanut reactions, but for the majority of the events triggered by other food. It is likely that other food triggers e.g. egg, milk are more common ingredients in non-prepacked food compared to peanut. However peanut was more likely to be listed as an ingredient, and the lower percentage of unknown data regarding labelling in the peanut cohort along with the lower consumption of non-prepacked food are hopefully indicative of a higher compliance to allergen avoidance in this group. A study on peanut-containing foods with precautionary labelling detected low levels of peanut in only two out of 38 products (18). Another study (19) reported detectable amounts of three allergens (peanut, milk and egg) in 5.3% of products with precautionary labelling and in 1.9% of products without. These issues still have to be addressed (20).

The interval between exposure and onset of symptoms was less than 10 minutes in the majority of cases, with no difference between peanut and other food, and with figures similar to previous analysis (21)(6).

Anaphylaxis appeared in a delayed pattern in a very small percentage of cases, again regardless of the food trigger.

Biphasic reactions were significantly more frequent in peanut anaphylaxis (10%) versus other food triggers (4%). The latter figure is in keeping with previous analysis of the children/adolescent cohort (5%) (6), and also with the NORA report on the mixed paediatric and adult population (4% in food induced anaphylaxis) (21). Similar (13) but also lower figures (22) were reported in other multicentre studies on paediatric anaphylaxis.

A possible link is with the higher frequency of severe anaphylaxis in the peanut cohort (65% grade III) versus the total children/adolescent cohort (47%) (6) or the mixed paediatric/adult cohort (38.3%) (21). However, there was no difference in reaction severity between the children who experienced a biphasic reaction and the ones who did not. Age 6 to 9 years was reported as one of five independent predictors for biphasic reactions (23), not confirmed in our data. Sometimes the prevalence of biphasic anaphylaxis is difficult to assess, depending on the time interval of patient observation post anaphylaxis, also symptoms occurring later might not be recognized as being related to the initial reaction. A systematic review and meta-analysis on predictors of biphasic analysis found food triggers to be associated with decreased risk for biphasic reactions (24).

Only 36% of the peanut anaphylactic reactions and 40% of the reactions triggered by other food were initially treated by a lay person, including self-administration of i.m. adrenaline. There was no statistically significant difference between subgroups regarding self-administration of i.m. adrenaline, but failure to apply/carry an adrenaline auto-injector was registered in 44% of peanut anaphylaxis and in 53% of the cases allergic to other food, which matches the reports of studies evaluating real-world use of AAI (25). In a community-based survey uncertainty about the severity of the reaction, fear of side effects, and difficulties deciding which drugs to use were identified as reasons for not applying AAIs (26).

Professional emergency treatment was mainly carried out by an emergency physician. Only 1 in 4 children with peanut anaphylaxis treated by a healthcare professional received adrenaline as first line treatment, despite the current guidelines reflecting strong expert opinion, that classifies i.m. adrenaline as first-line treatment of anaphylaxis (27). Surprisingly, professional administration of adrenaline (i.m., i.v., inhaled) was significantly higher in food anaphylaxis other than peanut compared to peanut anaphylaxis.

Despite recommendations, second- and third line drugs like antihistamines, steroids and beta 2-agonists were used as first-line drugs in the majority of the reactions, similar to other studies.

This supports a previous assertion that adrenaline is under-used in anaphylaxis treatment. A similar or lower proportion was reported for children and/or adults in other populations. Data from several cohort studies show the extent of under-treatment of anaphylaxis and the low rate of adrenaline use (27). US studies report higher usage of adrenaline in emergency setting, compared to Europe, with the majority of paediatric emergency medicine physicians (93.5%) correctly identifying adrenaline as first line treatment in anaphylaxis, yet only 66.9% choosing the i.m. route (28).

Aiming to evaluate the variation in the Emergency Department (ED) care of children with anaphylaxis, Michelson et al., 2016 (29) performed a retrospective cross-sectional study on data from 35 hospitals, on ED visits with a primary diagnosis of anaphylaxis over a period of 4 years, in children aged 1 month to 18 years. The least variation regarding adjunct therapies was observed in the use of H1-antihistamines and steroids, which were also the most frequent administered drugs. The study did not assess the frequency of adrenaline administration because it was assumed it is commonly given prior to hospital arrival.

Second-line treatment was required in less than 25% of professionally treated children (peanut cohort 24% vs other food cohort 19%), and a second dose of adrenaline was administered in 5% vs 6% (peanut vs other food). Recent data from the Registry showed that 3.7% of professionally managed anaphylaxis received a second dose of adrenaline (27), with higher figures in a mixed but smaller paediatric/adult cohort (13%; 18.5% for children only) (30).

Hospitalisation was higher in the peanut cohort, likely due to the difference in anaphylaxis severity (grade

III 65% vs 56%; p=0.001). Despite the fact that most cases were labelled as severe anaphylaxis, only 6% required admission to the Intensive Care Unit, and 0.7% had a fatal outcome.

Overall this data confirmed peanut as one of the major causes of severe, potentially life-threatening allergic reactions in children in Europe. Peanut anaphylaxis shows some characteristic features e.g. the presence of asthma comorbidity and the increased rate of biphasic reactions, conditions which may even be linked to each other. Clinicians should be aware of such characteristic findings for peanut allergy and consider these in the management of peanut anaphylactic patients.

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Table 1 Clinical profile of peanut versus other food induced anaphylaxis

	PEANUT	**PEANUT**	**OTHER FOOD**	**OTHER FOOD**	**p***
	n	%	n	%	

	PEANUT	**PEANUT**	**OTHER FOOD**	**OTHER FOOD**	**p***
Total	**459**	**100**	**1503**	**100**	
Boys	278	61	977	65	NS
0-6 years	282	61	975	65	NS
7-12 years	115	25	302	20	NS
13-17years	62	14	226	15	NS
Atopy	296	64	991	66	NS
Asthma	150	47	359	35	<0.001
Eczema	126	40	525	51	0.035
Rhinitis	115	36	343	33	NS
Food allergy	85	27	334	32	NS
Previous reactions	192	42	569	38	0.001
Milder	126	66	380	67	NS
Anaphylaxis	23	12	88	15	NS
Previous diagnosis[a]	167	45	409	33	<0.001
Cofactors	114	29	281	22	0.004
Exercise	91	80	215	77	0.002
Acute illness	16	14	36	13	NS
Severity R&M[e]					
Grade II	155	34	644	43	<0.001
Grade III	299	65	846	56	<0.001
Grade IV	5	1.1	13	0.9	<0.001
Non-prepacked[b]	123	31.7	610	63	0.005
Small eliciting amount[c]	197	66	446	43	<0.001
Biphasic reaction[d]	39	10	52	4	0.001

* Mann-Whitney *U* test

[a]based on n=371 as not known for n=88 and on n=1243 as not known for n=260

[b]based on n=320 as not known for n=138 and on n=972 as not known for n=531

[c]based on n=300 as not known for n=159 and on n=1034 as not known for n=469

[d]based on n=404 as not known for n=55 and on n=1314 as not known for n=189

[e]severity according to Ring&Messmer

n=number

NS=non-significant

Table 2 Emergency treatment and long-term management

	PEANUT	**PEANUT**	**OTHER FOOD**	**OTHER FOOD**	**p***
	n	%	n	%	
Total	**459**	**100**	**1503**	**100**	
First-line treatment	**407**	89	**1365**	91	NS
Solely lay	110	27	364	27	NS
Lay followed by professional	57	14	172	13	NS
Solely professional	240	59	829	61	NS
Emergency Physician[a]	119	40	440	44	NS
Self-administered i.m. adrenaline[b]	28	17	78	15	NS

	PEANUT	PEANUT	OTHER FOOD	OTHER FOOD	p*
Self-administered antihistamine[b]	106	63	426	79	<0.001
Self-administered steroids[b]	76	46	270	50	NS
Self-administered beta-2-agonists[b]	58	35	134	25	0.008
Professional adrenaline[c]	76	26	345	34	0.003
Professional antihistamine[c]	201	68	656	66	NS
Professional steroids[c]	220	74	704	70	NS
Professional beta-2-agonists[c]	91	31	247	25	0.044
Failure to use AAI[d]	22	44	89	53	NS
Second-line treatment[e]	93	24	248	19	NS
Second dose adrenaline	10	5	41	6	NS
Admission[f]	170	67	493	54	0.004
ICU	16	6	49	5	NS
Prophylaxis	**Prophylaxis**	**Prophylaxis**	**Prophylaxis**	**Prophylaxis**	**Prophylaxis**
Prescription of emergency drugs	446	97	1398	93	0.009
AAI	426	93	1246	89	0.003

* Mann-Whitney *U* test

[a]based on n=297 and n=1001 respectively, who received professional treatment

[b]based on n=167 and n=536 respectively, who received lay treatment

[c]aggregated adrenaline (i.m., i.v., inhaled), aggregated antihistamines (i.v., oral), aggregated steroids (i.v., oral, rectal), aggregated beta-2-agonists (i.v., oral, inhaled) based on n=297 and n=1001 respectively, who received professional treatment

[d]based on n=50 and n=167 respectively, who had AAI prescribed

[e]based on n=388 as not known for n=71 and on n=1279 as not known for n=224

[f]based on n=254 and n=920 respectively, where question was answered and information known

n=number

NS=non-significant

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