Original article

Anaphylactic reactions in children – a questionnaire-based survey in Germany

**Background:** Severe anaphylactic reactions are medical emergencies requiring immediate recognition and treatment. Despite this, little is known on their clinical features, especially in infants and children.

**Objective:** To evaluate trigger factors, patterns of clinical reaction, site of occurrence and treatment modalities of reported reaction in infants and children below 12 years of age in Germany.

**Methods:** Paediatricians throughout Germany were asked by questionnaire to report accidental anaphylactic reactions over the previous 12 months. Severity of reported reactions was classified in grades I–IV according to reported symptoms.

**Results:** Hundred and three cases of anaphylaxis were evaluated. Median age was 5 years, 58% were boys. Site of occurrence was the child’s home in the majority of cases (58%). Foods were the most common causative allergen (57%), followed by insect stings (13%) and immunotherapy (SIT) (12%); in 8% anaphylactic agent was unknown. Among foods, peanuts and tree nuts were the most frequent allergens (20% of food allergens in each case). Severe reactions with cardiovascular involvement occurred in 24% of cases. No fatal reaction was observed. Recurrent episodes of anaphylaxis were reported in 27% of cases, half of these caused by the same allergen again. For treatment, 20% of children received adrenaline, in 8% of cases intravenously. Thirty-six per cent of patients with grade-IV reactions received adrenaline, 24% intravenously. In 17% of all children an adrenaline self-injector was prescribed after the episode.

**Conclusion:** Our data: (i) shows an uncertainty of physicians in diagnosing anaphylaxis, (ii) reveals remarkable under-treatment of the majority of children with anaphylaxis, (iii) reflects the need for guidelines and training for physicians in managing children with anaphylaxis and (iv) should encourage the development of self-management programmes for patients and families.

Severe anaphylactic reactions are potentially life-threatening (1–7). In the literature, foods, venom and drugs are the most commonly reported exogenous causative agents (8, 9). Symptoms vary widely and can involve multiple organ systems, with cutaneous, gastrointestinal, respiratory, cardiovascular and/or unspecific signs and symptoms (8, 10–12).

In the paediatric population, allergic disorders have reached epidemic proportions (12), and anaphylaxis is an increasingly common event (8, 13, 14). Although it is a medical emergency requiring immediate recognition and treatment, there is a lack of information on its prevalence and characteristics, particularly in infants and children. Data on epidemiology of anaphylactic reactions is generally available only for selected groups. An accurate profile of the epidemiology of anaphylaxis would increase awareness of anaphylactic reactions among physicians for the recognition and treatment. However, such data is difficult to obtain.

The purpose of this questionnaire-based investigation was to describe the most important trigger factors, the pattern of clinical reaction, site of occurrence and treatment of anaphylactic reactions in infants and children in Germany.

**Methods**

In a retrospective study between October 2002 and December 2003, German paediatricians (clinicians and GP’s) were asked by circulars (sent out every 6 months) and by announcements in medical
Anaphylactic reactions in children – a Germany survey

Table 1. Classification of severity of reported anaphylactic reactions (grades I–IV) and frequency of occurrence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Symptoms</th>
<th>Severe</th>
<th>Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Local reaction (no systemic reaction)</td>
<td>Reddening, Induration, Itching, etc.</td>
<td>3 (3%)</td>
<td>22 (21%)</td>
</tr>
<tr>
<td>II</td>
<td>Mild systemic reaction (systemic reaction without cardiovascular or pulmonary involvement)</td>
<td>Urticaria, Flush, Angioedema, Abdominal pain, Nausea, Vomiting</td>
<td>53 (52%)</td>
<td>25 (24%)</td>
</tr>
<tr>
<td>III</td>
<td>Severe systemic reaction (systemic reaction with pulmonary symptoms but cardiovascular system stable)</td>
<td>Wheezing, Constriction in chest, Stridor, Dyspnea, etc.</td>
<td>100 (100%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Shock (cardiovascular collapse)</td>
<td>Dizziness*, Tachycardia*, Fall in blood pressure, Collapse, Shock, Cardiac/pulmonary arrest, etc.</td>
<td>25 (24%)</td>
<td></td>
</tr>
</tbody>
</table>

*Only in combination with other grade-IV symptoms.

Data processing and analysis was done with SPSS for Windows (Version 11.5). The Mann–Whitney U-test and chi-square analyses were used to test for statistical correlation. A P < 0.05 was considered significant.

Results

Study population

Hundred and three anaphylactic reactions reported from 93 paediatricians met the inclusion criteria and were evaluated. About 21/93 reporting physicians were from paediatric clinics, 72/93 were paediatric GP’s. Patients’ age ranged from 3 months to 12 years (median 5 years), 60/103 (58%), were boys and 43/103 (42%) girls. About 46% (45%) children suffered from bronchial asthma, 47 (46%) from atopic dermatitis, 34 (33%) from food allergies and 10 (10%) from allergic rhinoconjunctivitis.

Site of occurrence

The most common site of occurrence was in the child’s home (58%) (Fig. 1). Ten per cent of all episodes occurred at school or kindergarten, and 10% on the street or other public places, while 14% happened in a medical setting like a practice or hospital (12% due to SIT, 1% due to a drug, and 1% due to a skin-prick test); 8% occurred elsewhere.

Table 2. Frequency of reported causative allergens for anaphylaxis

<table>
<thead>
<tr>
<th>Food</th>
<th>Insect sting</th>
<th>SIT</th>
<th>Medication</th>
<th>Other*</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>All allergens (n = 103)</td>
<td>13 (13%)</td>
<td>12 (12%)</td>
<td>6 (6%)</td>
<td>4 (4%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Peanut</td>
<td>12 (20%)</td>
<td>12 (20%)</td>
<td>8 (14%)</td>
<td>8 (14%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>8 (14%)</td>
<td>8 (14%)</td>
<td>4 (7%)</td>
<td>15 (25%)</td>
<td></td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>10%</td>
<td>10%</td>
<td>8%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>Hen’s egg</td>
<td>10%</td>
<td>10%</td>
<td>8%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>10%</td>
<td>10%</td>
<td>8%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>Other*</td>
<td>10%</td>
<td>10%</td>
<td>8%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>10%</td>
<td>10%</td>
<td>8%</td>
<td>58%</td>
<td></td>
</tr>
</tbody>
</table>

*Lesser than or equal to two cases per allergen.
There were significant age differences between the groups of children affected by the various causative agents. While children with reported food related anaphylaxis were significantly younger than the overall group (mean age, SD = 3.9 ± 3.0), those with SIT dependent and venom dependent anaphylaxis were significantly older (9.8 ± 1.9 and 7.6 ± 3.2, respectively) (Fig. 2).

Diagnostic tests

In 70 (68%) cases, allergy testing was performed to identify the anaphylactic agent, while in 26 (25%) cases no allergy testing was done at all. For the remaining 7/103 cases (7%) no information was provided. Specific Immunoglobulin E (IgE) concentrations in serum were determined in 63 children (45 positive, seven negative and 11 unknown results) and/or skin-prick tests were performed in 28 cases (19 positive, five negative and four unknown results). Ten children went through an allergen-provocation (in five cases with a positive result, three negative and two unknown) and four children underwent atopy-patch-testing (one positive, two negative and one unknown result).

Clinical symptoms

Independent of severity grading, 92% of all children showed cutaneous signs or symptoms. Respiratory involvement was found in 75% of the children and cardiovascular symptoms in 46%; the gastrointestinal tract was involved in 36% of all episodes. Graduating severity, in 3% of all cases reported symptoms were classified as local (grade-I reaction), and 21% as mild systemic reaction (grade II) (Table 1). Fifty-two per cent of all episodes were classified as severe systemic reaction (grade III). Twenty-four per cent of children experienced episodes with cardiovascular shock symptoms (grade IV). Considering only grades III and IV reactions, beside respiratory and/or cardiovascular symptoms an involvement of the skin was found in 91% of cases. One near-fatal reaction was reported, but there were no fatalities.

Recurrent reactions

In 28 cases (27%) the reported symptoms were already a recurrent episode. Twenty of these actual reactions (71%) were food-related, 2 (7%) occurred after an insect sting and two after SIT. In four children, the causative allergen was unknown. In 50% the recurrent episode was due to the same allergen as the anaphylactic episode(s) in medical history.

Treatment

Most of the children were treated with corticosteroids (80%), antihistamines (72%) and/or β2-agonists (72%). Adrenaline was used in 20% of all cases, 8% intravenous (i.v.), 1% subcutaneous (s.c.) and 12% by inhalation. No patient received intramuscular adrenaline. Seven per cent got i.v. fluids and 8% were not treated at all. Treatment in more detail and according to severity of reported anaphylaxis is shown in Table 3.

Drugs were administered to 32 children (30%) first by a nonhealth care professional, mostly by their parents (30 cases), two of them by a teacher. In these cases, oral antihistamines were used for treatment in 26 cases, rectal corticosteroids in 22 and inhaled steroids in two cases. Seven children received β2-agonists by inhalation and two of them inhaled adrenaline.

An epinephrine self-injector had already been prescribed in only 1 of the 28 patients with recurrent episodes of anaphylactic reactions, but it was not used in the reported severe systemic reaction (grade III). In all, 53 children (52%) were admitted to hospital: 15 out of 25 children with grade-IV reaction, 24/53 grade III, 11/22 of grade II and 3/3 grade-I reactions.

Emergency set

About 78 (77%) of the children were given ‘emergency equipment’ for first-aid treatment after the reported episode of anaphylaxis: 17 got an adrenaline-self-injector, one adrenaline for s.c. injection, and 19 adrenaline for inhalation. In all other cases antihistamines, steroids and/or β2-agonists were prescribed. Twenty-nine of the children were prescribed three different medications for intervention in the case of emergency, and two patients were given four different medications.
**Table 3. Medical treatment according to grades I–IV anaphylaxis**

<table>
<thead>
<tr>
<th>Grade</th>
<th>I (3)</th>
<th>II (22)</th>
<th>III (52)</th>
<th>IV (25)</th>
<th>Total (102)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 agonists</td>
<td>0</td>
<td>0</td>
<td>15 (28%)</td>
<td>6 (24%)</td>
<td>21 (21%)</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>2 (67%)</td>
<td>15 (68%)</td>
<td>36 (68%)</td>
<td>20 (80%)</td>
<td>73 (72%)</td>
</tr>
<tr>
<td>Steroids</td>
<td>3 (100%)</td>
<td>13 (60%)</td>
<td>44 (83%)</td>
<td>22 (88%)</td>
<td>82 (80%)</td>
</tr>
<tr>
<td>Adrenaline (i.v./inhaled/s.c.)</td>
<td>1 (0%/1/0) (33%)</td>
<td>3 (1/2/1)† (14%)</td>
<td>7 (1/6/0) (13%)</td>
<td>9 (6/3/0) (36%)</td>
<td>20 (8/12/1)† (20%)</td>
</tr>
<tr>
<td>Intravenous fluids</td>
<td>0</td>
<td>0</td>
<td>4 (8%)</td>
<td>3 (12%)</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>No therapy</td>
<td>0</td>
<td>3 (6%)</td>
<td>3 (6%)</td>
<td>2 (8%)</td>
<td>8 (8%)</td>
</tr>
</tbody>
</table>

*In one reported case, the therapy was unknown.
†One patient was treated with both inhalant and subcutaneous adrenaline.

**Discussion**

Our survey confirms that anaphylaxis in childhood is mostly triggered by foods and occurs in an out-of-hospital setting in the majority of cases. Furthermore, it demonstrates that most of the children did not receive adequate treatment.

This is the first nation-wide investigation of anaphylaxis in infants and children in Germany. We aimed at performing a study in young children, and not in adolescents, which probably show a different pattern of clinical reactions, e.g. in terms of pollen-associated food allergies. Furthermore, the study was not designed as an epidemiological cross-sectional survey of the general paediatric population. It rather is a collection of cases seen by paediatricians in daily practice and hospital, without a selection of only hospitalized children or children seen in a specialist centre as published in other investigations of childhood anaphylaxis (12, 14, 15). Reactions as a result of allergen provocation were excluded.

In our retrospective design, we asked for the suspected etiologic agent of anaphylaxis. This was reported by the physicians in the questionnaire, and was not proven by allergy tests in the majority of cases. In a prospective study, *in vivo* or *in vitro* tests or provocation tests would be the method of choice to ensure a causing agent (16, 17). The fact of a retrospective survey may possibly bias towards reporting of more severe reactions. However, this is not likely since evaluation of the questionnaire revealed that one quarter (24%) was classified as grade I or II.

Remarkably, nine paediatricians volunteered information that they had not seen a case of anaphylaxis in a child, underlining the rare character of this medical emergency and the challenge for every medical career faced with such a situation.

Skin symptoms (92%) and respiratory (75%) symptoms were more frequent than gastrointestinal (36%) and cardiovascular ones (46%). This is in accordance with other investigations of anaphylaxis in children (8, 12, 14) where skin symptoms vary from 78 to 93%, respiratory involvement from 69 to 93% and gastrointestinal symp-
References


Acknowledgments

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