Paediatric anaphylaxis: a 5 year retrospective review

Objective: To describe the demographic characteristics, clinical features, causative agents, settings and administered therapy in children presenting with anaphylaxis.

Methods: This was a retrospective case note study of children presenting with anaphylaxis over a 5-year period to the Emergency Department (ED) at the Royal Children’s Hospital, Melbourne.

Results: One-hundred and twenty-three cases of anaphylaxis in 117 patients were included. There was one death. The median age of presentation was 2.4 years. Home was the most common setting (48%) and food (85%) the most common trigger. Peanut (18%) and cashew nut (13%) were the most common cause of anaphylaxis. The median time from exposure to anaphylaxis for all identifiable agents was 10 min. The median time from onset to therapy was 40 min. Respiratory features were the principal presenting symptoms (97%). Seventeen per cent of subjects had experienced anaphylaxis previously.

Conclusions: This is the largest study of childhood anaphylaxis reported. Major findings are that most children presenting to the ED with anaphylaxis are first-time anaphylactic reactions and the time to administration of therapy is often significantly delayed. Most reactions occurred in the home. Peanut and cashew nut were the most common causes of anaphylaxis in this study population, suggesting that triggers for anaphylaxis in children have not changed significantly over the last decade.

Anaphylaxis is predominately a childhood disease, estimated to occur in one out of 170 children (1) compared to 30 per 100 000 person-years in adults (2); however, most studies reporting on the clinical features and causes have focused on adult or combined adult and paediatric populations (3–15). This may relate to the finding that most deaths from anaphylaxis occur in people over 10 years of age (16–18). Whilst it has been reported that cases of severe anaphylaxis overwhelmingly present to the Emergency Department (ED) for treatment (24), in the last decade, only one small study has focused specifically on paediatric anaphylaxis in the emergency setting; a study of 57 children (upper age of 15 years) presenting with anaphylaxis to a Paediatric ED in Queensland, Australia (19). This study found that food is the most common trigger for anaphylaxis in children and that respiratory features predominate in children, compared to mixed cardiovascular and respiratory features in adults. A small number of other studies have also looked specifically at paediatric anaphylaxis in other settings (e.g. general paediatrician patients, hospital inpatients, a specialist allergy centre). Food is often reported as the most common trigger and the home being the most common site of reaction (1, 20–22).

This study of 123 cases of paediatric anaphylaxis presents a more comprehensive review that expands on previous findings and identifies new information; that most children presenting to ED with anaphylaxis are first-time reactions and that administration of therapy is often significantly delayed, most reactions occur in the home, and peanut and cashew nut are the most common triggers. The findings have significant implications for the management and treatment of childhood anaphylaxis.

Methods

Patient selection

This was a retrospective case note study of children presenting with anaphylaxis to the ED at the Royal Children’s Hospital (RCH), Melbourne, Australia, over a 5-year period from 1 June 1998 to 30 June 2003. The upper age of presentation to RCH ED is 18 years.

Cases were identified from the medical record database using the codes anaphylactic shock caused by adverse food reaction (T78.0), anaphylactic shock excludes reactions caused by food or vaccine (T78.2), allergy unspecified (T78.4) and other adverse food reactions not elsewhere classified (T78.1). It should be noted that diagnosis is
recorded on the database by the treating doctor and then the appropriate code is assigned by clerical staff. Criteria for inclusion in the study were children with (i) a diagnosis of anaphylaxis and (ii) not on any concurrent beta-blockade, corticosteroid or anti-histamine therapy. Children on such therapy were excluded as a result of the potential that these medications could influence the natural history of an anaphylactic reaction. Ethics approval was obtained prior to reviewing patient records.

Definitions

The definitions for anaphylaxis and a generalized allergic reaction used in the study are those currently agreed upon internationally (23, 24). Patient files were reviewed by the investigators to ensure that the clinical signs recorded were consistent with a diagnosis of anaphylaxis as recorded on the medical database. Anaphylaxis was defined as a multi-system allergic reaction characterized by (i) one or more clinical features involving the respiratory and/or cardiovascular system (CVS) associated with and (ii) one or more clinical features involving the skin and/or gastrointestinal tract (GIT). A generalized allergic reaction was defined as an allergic reaction characterized by one or more symptoms or signs involving the skin and/or GIT without involvement of either the CVS or respiratory systems. Cardiovascular system features identified were hypotension, loss or impairment of conscious state and pule and floppy presentation in an infant. Hypotension was defined as a systolic blood pressure less than the calculated normal blood pressure for age (80 mmHg + age × 2). Respiratory features identified were difficulty or noisy breathing, swelling of the tongue, swelling or tightness of the throat, difficulty talking, hoarse voice, stridor, wheeze, persistent cough and tachypnea. Gastrointestinal features identified were abdominal pain, vomiting and diarrhoea and skin features identified were angioedema, urticaria, generalized prurius and erythema.

Items identified during the chart review were demographic characteristics, past medical history, medication history, setting and type of allergen exposure, presenting clinical features, therapy instituted, hospital progression and the location of management of the initial anaphylactic reaction. A hospital admission was deemed one that required observation for >6 h.

Statistical analysis

Data was analysed using MINITAB for Windows (Minitab Inc., State College, PA, USA). Continuous data was described as either mean (SD) or median [interquartile range (IQR)] if not normally distributed. Differences between groups for categorical variables were determined using either the chi-square analysis or Fisher’s Exact test. The Mann–Whitney U-test or Student’s t-test was used for comparisons between nonparametric and parametric continuous variables respectively. Confidence intervals (95%) around values were determined by the Confidence Interval Analysis program (Professor Martin Gardner, UK, Version 1.0). P-values < 0.05 were considered statistically significant.

Results

Overview

There were a total of 181 allergic episodes that presented to the ED. Fifteen cases were excluded because of concomitant corticosteroid (n = 2) or anti-histamine use (n = 1), patient file unavailable (n = 3) and coding errors (n = 9). One-hundred and sixty-six episodes remained for analysis. Of these, 43 had generalized allergic reactions (in 42 children) and 123 had anaphylactic reactions (in 117 children).

Age and sex

The 123 anaphylaxis cases occurred predominantly in males (n = 77, 63%). The median age of presentation was 2.4 years (IQR 1.4–6.6) (Table 1). There was no statistically significant difference between males and females with respect to the age of presentation, trigger of anaphylaxis or presenting clinical features.

Allergic disease

A history of allergic disease at presentation was common. Out of the 117 children presenting to hospital, 47 had eczema (40%), 38 had asthma (32%) and 10 (9%) had symptoms of rhinitis. Fifteen of the 38 patients (54%) with asthma were on a preventer inhaler at the time of presentation. Children with asthma were as likely to present with respiratory or cardiovascular features of anaphylaxis compared to those without asthma. The presence of asthma was not associated with more severe anaphylaxis, with similar number of adrenaline boluses and i.v. fluid boluses in children with or without asthma. Children with asthma were, however, more likely to require oxygen (P < 0.05) and ventolin (P < 0.05) during anaphylaxis.

Setting and allergens

Home was the most common setting of anaphylaxis (Table 2), whilst food was the most common trigger (Table 3A). Peanuts accounted for 18% of food reac-
Tions. Tree nuts closely followed causing 17% of food reactions. Of the tree nuts, cashew nuts were by far the most common (14/18) (Table 3B). Drugs and insect stings accounted for the remaining anaphylaxis episodes (Table 3A). The drugs were aspirin (n = 1), amoxicillin and clavulanic acid (n = 1), cefaclor (n = 2), cephalexin (n = 1), topical fluorescein eye drops (n = 1) and undefined anaesthetic agents (n = 1). Out of the 117 children, only 20 (17%) had a past history of anaphylaxis, and in six of the 20 cases the current anaphylaxis episode related to the same allergen that had caused anaphylaxis previously.

The median time from exposure to anaphylaxis for all identified agents was 10 min (IQR: 5–60). Food anaphylaxis presented at an earlier age than both drug (median age 2 years vs 13 years P = 0.0005) and insect stings (median age 2 years vs 9 years P = 0.04). Whilst food appeared to induce anaphylaxis more rapidly than drug and insect stings (Table 3A), the differences in the median time to induce anaphylaxis for food, drug and insect did not reach statistical significance.

Clinical features of anaphylaxis

During the initial anaphylaxis episode, respiratory features dominated (n = 119/123, 97%), followed by skin (n = 119/123, 97%), GIT (n = 36 123, 29%) and CVS signs (n = 21/123, 17%) (Table 4A). Gastrointestinal tract features were more likely to be associated with CVS than respiratory signs (P < 0.05) (Table 4B). Skin features were more frequently associated with respiratory than with CVS signs alone (P < 0.05) (Table 4B).

Therapeutic interventions

The treatments administered during the initial anaphylactic reaction are shown in Table 5. The admission rate for anaphylactic cases was 83% (n = 102/123), with a median length of stay being 17 h (12–22).

Mortality

There was one fatality (1%) over the 5-year period. This was a 7-year-old girl who ingested a peanut satay sauce.
de Silva et al.

Table 5. Therapy administered at initial anaphylaxis (n = 123)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>n (%)</th>
<th>Median time (min) between anaphylaxis onset and initial dose*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number who had adrenaline</td>
<td>94 (76)</td>
<td>40 (23–78)</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>52 (56)</td>
<td></td>
</tr>
<tr>
<td>Intravenous</td>
<td>6 (6)</td>
<td></td>
</tr>
<tr>
<td>Intramuscular</td>
<td>31 (33)</td>
<td></td>
</tr>
<tr>
<td>Not stated</td>
<td>5 (5)</td>
<td></td>
</tr>
<tr>
<td>If no adrenaline administered why?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number</td>
<td>29 (24)</td>
<td></td>
</tr>
<tr>
<td>Indicated based on history, but not given</td>
<td>22 (76)</td>
<td></td>
</tr>
<tr>
<td>Symptoms resolved by time of medical care</td>
<td>6 (21)</td>
<td></td>
</tr>
<tr>
<td>Parental refusal</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Steroid administered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administered</td>
<td>95 (77)</td>
<td>90 (66–138)</td>
</tr>
<tr>
<td>Anti-histamines Administered</td>
<td>73 (59)</td>
<td>90 (42–132)</td>
</tr>
<tr>
<td>Other therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen administered</td>
<td>36 (29)</td>
<td></td>
</tr>
<tr>
<td>Bolus normal saline</td>
<td>13 (11)</td>
<td></td>
</tr>
<tr>
<td>Volume of normal saline (ml/kg)</td>
<td>13 (2–42)</td>
<td></td>
</tr>
<tr>
<td>Inhaled salbutamol</td>
<td>39 (32)</td>
<td></td>
</tr>
<tr>
<td>Adrenaline infusion</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>2 (2)</td>
<td></td>
</tr>
</tbody>
</table>

*P = 0.0001 for adrenaline vs steroids or anti-histamines.

with known nonanaphylactic peanut allergy in the past. This was on a background of severe eczema requiring topical steroids (mometasone furoate) and asthma needing a preventer (sodium cromoglycate) three times a day with ongoing frequent mild symptoms. Intravenous adrenaline was administered 20 min after symptom onset by paramedics. Intubation and multiple doses of parenteral adrenaline were required but without any period of symptom control.

Discussion

The major new findings identified by this study are that most children presenting to the ED with anaphylaxis are first-time anaphylactic reactions and that the time to administration of therapy is often significantly delayed. The study also found that most reactions occurred in the home, a finding supported by paediatric studies that have used other methods of patient selection (1, 20, 21), and that peanut and cashew nut were the most common causes of anaphylaxis in this study population, a finding similar to the one described by Pumphrey and Stanworth in 1996 (12) suggesting that triggers for anaphylaxis in children have not changed significantly over the last decade.

To date there have been few papers published focusing exclusively on the demographics of paediatric anaphylaxis and historically there have been inconsistencies in the definition of anaphylaxis which has made it difficult for researchers to compare results. This study examined all presentations of anaphylaxis to a major paediatric ED over a 5-year period (1998–2003) and represents the largest study of the clinical features and causative agents of childhood anaphylaxis reported. The RCH ED is the largest dedicated paediatric ED in the state of Victoria and is likely to have seen the majority of cases of children’s anaphylaxis presenting to ED over that time period (25).

The definition of anaphylaxis used to identify subjects is consistent with international consensus definitions (23, 26) where the presence of either cardiovascular and/or respiratory symptoms indicates classification as anaphylaxis.

There has been one similar study conducted previously in Australia (using the same definition of anaphylaxis) that reviewed all allergic presentations to a paediatric ED over a 3-year period (1998–2001) (19). Our study supports their main finding that respiratory symptoms predominate over CVS symptoms in childhood anaphylaxis.

Surprisingly penicillin was not the predominate drug causing anaphylaxis in contrast to previous reports (4, 10, 27, 28). This may be as a result of a small sample of subjects with drug-induced anaphylaxis in this study.

The majority of children presenting to the ED with anaphylaxis are first-time anaphylactic reactions.

In this study, the majority of children presenting to the ED with anaphylaxis had not experienced anaphylaxis before (only 17% had previous anaphylaxis). It was not recorded whether the subjects knew that they were allergic to the precipitant that caused anaphylaxis; however, other anaphylaxis studies of adults and children have recorded the number of subjects with a known allergy to the causative allergen as being relatively low, from 19% to 28% (4, 14, 15, 19).

Currently in Australia, anaphylaxis prevention and management strategies are implemented following diagnosis of anaphylaxis and centre around allergen avoidance and prescription of an EpiPen for emergency management. This approach does not cater for the majority of children and adults who experience first-time anaphylaxis and have not been identified as being at risk of anaphylaxis.

In the absence of a ‘cure’ for anaphylaxis the identification of risk factors plays an important role in prevention. Our study and other studies have highlighted that the presence of other allergic disorders is a particularly strong risk factor for anaphylaxis in young children (12) and in those with food allergy (7, 12).

It was interesting that in this study asthma was only observed in 32% of patients presenting with nonfatal anaphylaxis, whereas in studies of fatalities, symptomatic asthma was noted in a majority of cases (16, 18, 29). This supports the notion that asthma, particularly if there are active symptoms, is indeed a risk factor for fatal anaphylaxis.
The onset of anaphylaxis is quick, however, the administration of treatment is slow and not always in line with best practice therapy

Although the clinical features of anaphylaxis developed quickly (10 min) it took a long time, a further 40 min, for first line therapy (adrenaline) to be administered to the children in the study (Table 5). Whilst there was only one fatality in this study group (who received adrenaline 20 min after onset of symptoms), this finding highlights the limited ability of the community to effectively deal with severe and potentially life-threatening anaphylaxis in children.

Adrenaline is the appropriate initial management for anaphylaxis; however, medical services do not always deliver optimal therapy. One Australian paediatric ED reported adrenaline administration in children with confirmed anaphylaxis in only 26% of cases (19). In our study, 85% of children received some form of adrenaline, however, the primary mode of delivery was s.c. (52% of children). It is accepted that the s.c. route is not the optimal route of administration (30), especially in the hypotensive child where systemic absorption of the drug is likely to be impaired.

Peanuts and cashew nuts are the most common cause of anaphylaxis in children

Food allergy was found to be the most common cause of anaphylaxis in children, a finding that is supported by other studies that have included children in their study populations (12, 19, 27).

However, the type of food causing food-induced anaphylaxis was strikingly different in our study when compared to the similar, previous study by Braganza et al. (19). Peanut (18%) and tree nuts (17%), largely cashew nuts (14/18) stood out as the most common cause in our study (Table 3B), a finding supported by other studies in and outside of Australia (1, 12, 31) whereas egg and dairy were the most common cause of food induced anaphylaxis (47%) in the Queensland paediatric study.

The reason why nuts appear to be causing the majority of food-related anaphylaxis in this study while egg is generally reported as the most common cause of food allergy (31) may be that peanuts and tree nuts are more potent allergens. Pumphrey (25) noted that lower doses of peanut caused a fatal reaction than other foods (median dose peanut = 1 g, median dose other foods = 10 g). Studies have identified that cashew nut may be an even more potent allergen than peanut (32, 33) and that whilst peanut allergy is more common than cashew nut allergy, children with cashew nut allergy are more likely to have anaphylaxis. Further research is required to confirm the hypothesis that peanuts and cashew nuts are more potent allergens.

There are limitations of this study related to its retrospective design and the lack of inclusion of children with respiratory signs alone; however, this is considered a rare presentation of anaphylaxis. Inherent to any retrospective analysis is the potential for inadequate or incomplete documentation, for example missing data because of the lack of systemic approach to documentation by different doctors. For example, 29% of subjects in this study did not have the setting of anaphylaxis recorded. Anaphylaxis can present with isolated respiratory signs (34, 35). Although in this study no child presented in this manner, the current definitions of anaphylaxis would not include these patients. The codes used to identify subjects could possibly lead to over-representation of food allergy, however, we believe the inclusion of the T78.2 code (anaphylactic shock excluding reactions because of food or vaccine) and the T78.4 code (allergy unspecified) would have identified all cases of drug (except immunotherapy) or insect anaphylaxis presenting to the ED during the period of the study.

Conclusion

Our study supports previous reports that food is the most common trigger for anaphylaxis in children, and that respiratory features predominate in children compared to mixed cardiovascular and respiratory features in adults. New findings of our study relating to children presenting to an ED are that (i) the most children presenting to the ED with anaphylaxis are first-time anaphylactic reactions; (ii) the time to administration of therapy is often significantly delayed; (iv) the most common setting for anaphylaxis is in the home and (iv) peanut and cashew nut were the most common causes of anaphylaxis in this study population, a finding similar to the one described by Pumphrey and Stanworth in 1996 (12) suggesting that triggers for anaphylaxis in children have not changed significantly over the last decade.

References


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1075


