

ORIGINAL ARTICLE

Clinical predictors for biphasic reactions in children presenting with anaphylaxis

S. Mehr^{1*,†}, W. K. Liew^{1*,‡}, D. Tey^{*} and M. L. K. Tang^{*,§,¶}

^{*}Department of Allergy and Immunology, Royal Children's Hospital, Melbourne, Australia, [†]Discipline of Paediatrics and Child Health, The Children's Hospital at Westmead Clinical School, University of Sydney, Sydney, Australia, [‡]Department of Paediatric Allergy, Immunology and Rheumatology, KK Women's and Children's Hospital, Singapore, Singapore, [§]Allergy and Immune Disorders, Murdoch Children's Research Institute, Melbourne, Australia and [¶]Department of Paediatrics, University of Melbourne, Melbourne, Australia

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Summary

Background One of the main reasons for hospital admission once a child has been stabilized following anaphylaxis is to monitor for a biphasic reaction. However, only a small percentage of anaphylactic episodes involve biphasic reactions that would benefit from admission. Identification of predictive factors for a biphasic reaction would assist in determining who may benefit from prolonged observation.

Objective To determine predictive factors for biphasic reactions in children presenting with anaphylaxis.

Methods This was a retrospective study of children presenting with anaphylaxis to a major paediatric emergency department over a 5-year period.

Results There were 95 uniphasic (87%), 12 (11%) biphasic and two protracted reactions (2%). One child with a protracted reaction died. For the management of the primary anaphylactic reaction, children developing biphasic reactions were more likely to have received > 1 dose of adrenaline (58% vs. 22%, $P = 0.01$) and/or a fluid bolus (42% vs. 8%, $P = 0.01$) than those experiencing uniphasic reactions. The absence of either factor was strongly predictive of the absence of a biphasic reaction (negative predictive value 99%), but the presence of either factor was poorly predictive of a biphasic reaction (positive predictive value of 32%). All biphasic reactors, in which the second phase was anaphylactic, received either > 1 dose of adrenaline and/or a fluid bolus.

Conclusions Children who received > 1 dose of adrenaline and/or a fluid bolus for treatment of their primary anaphylactic reaction were at increased risk of developing a biphasic reaction.

Keywords anaphylaxis, biphasic, children

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Correspondence:

Assoc. Prof. Mimi Tang, Department of Allergy and Immunology, Royal Children's Hospital, Melbourne, Flemington Road, Parkville, Vic. 3052, Australia.
E-mail: mimi.tang@rch.org.au

Introduction

Anaphylaxis is an immediate, potentially life threatening hypersensitivity reaction that can be classified as being uniphasic (single episode), biphasic (second reaction after initial recovery) or protracted (no initial recovery period) [1]. The prevalence of biphasic reactions in children following anaphylaxis has been reported in one study to be 6% [2]. Other retrospective studies performed in adult or mixed adult–paediatric populations have reported si-

milar biphasic rates [1, 3, 4], with higher rates often noted in prospective studies [5, 6]. Reports that some biphasic reactions are more severe than the initial anaphylactic reaction have caused concern [7, 8], with some authors recommending a 24-h period of hospital observation for all patients presenting with anaphylaxis [8, 9]. Yet the majority of patients admitted following anaphylaxis do not receive further treatment and are discharged after overnight observation [2]. Clinical characteristics of biphasic anaphylaxis and predisposing factors have been summarized and reviewed recently [9, 10]. Only one previous study has examined biphasic reactions in

[†]Contributed equally to the preparation of this manuscript.

children [2]. The ability to accurately predict the likelihood of a biphasic reaction based on clinical signs and/or the severity of the initial anaphylactic reaction would be ideal. However, no clinical feature has been consistently shown to be predictive of a biphasic response, and there is often a lack of consistency between studies regarding identified biphasic risk factors. The aim of this study was to investigate the prevalence of the biphasic response and predictive factors for biphasic reactions in children admitted with anaphylaxis.

Methods

Patient selection

This was a retrospective case note study of children presenting with anaphylaxis to an Emergency Department (ED) at the Royal Children's Hospital (RCH), Melbourne, Vic., Australia, over a 5-year period from 1 June 1998 to 30 June 2003. The demographic characteristics of childhood anaphylaxis in this population have been published separately [11]. RCH is a major tertiary paediatric hospital and its ED represents the only dedicated paediatric ED in the state of Victoria.

Potential cases of anaphylaxis were identified from the medical record database using the International Classification of Diseases (ICD) version 10 – Australian Modification (ICD-10-AM) codes: anaphylactic shock due to adverse food reaction (T78.0), anaphylactic shock unspecified (T78.2), anaphylactic shock due to serum (T80.5), anaphylactic shock due to adverse effects of drugs properly administered (T88.6), allergy unspecified (T78.4) and other adverse food reactions not elsewhere classified (T78.1). Children were included if they were admitted into hospital for >6 h (as per the definition of an admission used by the RCH emergency department) with a diagnosis of anaphylaxis, and were not receiving before their reaction, any daily β -blockade, corticosteroid, immunosuppressant and/or antihistamine therapy. Children on such therapies were excluded due to the potential that these medications could influence the natural history of an anaphylactic reaction.

Definitions

Anaphylaxis was defined as a multi-system allergic reaction characterized by one or more clinical features involving the respiratory and/or cardiovascular system (CVS) associated with one or more clinical features involving the skin and/or gastrointestinal tract (GIT), as described by the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network (NIAID/FAAN) consensus definitions [12]. A non-anaphylactic allergic reaction was defined as a reaction characterized by one or more symptoms or signs involving the skin and/or GIT without

involvement of either the CVS or respiratory systems [13]. Clinical features were defined as CVS (hypotension, loss or impairment of conscious state, pale and floppy presentation in an infant), respiratory (difficulty or noisy breathing, swelling of the tongue, swelling or tightness of the throat, difficulty talking, hoarse voice, stridor, wheeze, persistent cough, tachypnea), GIT (abdominal pain, vomiting, diarrhoea) and skin (angioedema, hives, urticaria, generalized pruritus, erythema) [13]. Hypotension was defined as a systolic blood pressure less than the estimated normal blood pressure for age ($80 \text{ mmHg} + (\text{age} \times 2)$ for children between 1 and 12 years of age; and $100 \text{ mmHg} + \text{age}$ for those >12 years of age) [14]. Items identified in the chart review included – demographic characteristics, past medical history, medication history, setting and type of allergen exposure, presenting clinical features, therapy instituted and hospital progression. Ethics approval was obtained before reviewing patient records. The management of the initial anaphylactic reaction occurred either in an ambulance, general practitioner's office, local hospital ED or the Royal Children's Hospital ED.

Some children had their initial adrenaline dose administered via an EpiPen (Commonwealth Serum LaboratoriesTM, Parkville, Australia) by their parent. Consequently, the therapy provided for each patient was based on the judgment of the individual physician, ambulance officer or parent. A biphasic reaction was defined as an initial anaphylactic reaction with a period of resolution for ≥ 1 h, during which there were no new symptoms or treatment administered, followed by a second phase anaphylactic or non-anaphylactic allergic reaction, not caused by antigen re-exposure. A protracted reaction was defined as an anaphylactic reaction without an interval period of resolution associated with CVS symptoms or signs. The severity of the biphasic reaction was assessed as being less severe (i.e. second reaction was a non-anaphylactic reaction), of similar severity (i.e. second reaction was an anaphylactic reaction) or more severe than the initial event (i.e. second reaction was an anaphylactic reaction requiring more aggressive therapy, such as an adrenaline infusion and/or intubation).

Statistical analysis

Data were analysed using Minitab 15.1 (Minitab Inc., State College, PA, USA). Continuous data were described as the mean (standard deviation) or median (range) for parametric and non-parametric data, respectively. The Student *t*-test or Mann-Whitney U-test were used for comparisons between parametric and non-parametric continuous variables, respectively. Differences between groups for categorical variables were determined using either the Chi-square analysis or Fisher's exact test. Sensitivity, specificity, positive predictive value (PPV) and negative

predictive value (NPV) were calculated as described elsewhere [15]. Confidence intervals (95% CI) were determined by the Confidence Interval Analysis programme (Version 1.0, Professor Martin Gardner, UK). *P*-values <0.05 were considered statistically significant.

Results

Demographics

A total of 145 anaphylactic episodes in 138 children were identified during the study period. Twenty-three episodes were excluded as they were observed for <6 h (range 0.9–4.4 h) and discharged directly from the RCH emergency department. A further 13 episodes were excluded due to daily use of chemotherapeutic or biological agents (*n* = 10), corticosteroids (*n* = 2) or antihistamines (*n* = 1) before the anaphylactic reaction. One hundred and nine episodes of anaphylaxis occurring in 104 children were eligible for inclusion. There was a male predominance (*n* = 62/104, 60%) and the median age of children was 2.5 years (0.2–18.8). There were 95 (87%) uniphasic reactions in 90 children, 12 (11%) biphasic reactions in 12 children and two (2%) protracted reactions in two children. There was one death (in one of the children with a protracted reaction). The demographic characteristics, past medical histories, anaphylaxis presentation, triggers, and treatment were compared between uniphasic and biphasic cases.

Clinical predictors for biphasic and uniphasic reactions

Demographics and atopic history. There were no significant differences between the two groups with respect to age at the initial anaphylaxis presentation, gender, presence of atopic disease or a past history of anaphylaxis (Table 1).

Table 1. Demographic characteristics of children with biphasic (*n* = 12) vs. uniphasic (*n* = 90) reactions

Demographics	Biphasic (<i>n</i> = 12)	Uniphasic (<i>n</i> = 90)	<i>P</i> value
Males (%)	8 (67%)	53 (59%)	0.76
Median age of presentation in years	9.6 (0.2–16.7)	2.4 (0.2–18.8)*	0.10
Presence of any atopic disease (%) [†]	7 (58%)	52 (58%)	1.0
Asthma	3 (25%)	28 (31%)	1.0
Past history of anaphylaxis (%)	2 (17%)	10 (11%) [‡]	0.62

*One patient was 18.8 years of age at the time of admission. All other patients were < 18 years of age.

[†]Atopic disease, current history of asthma, eczema and/or allergic rhinitis.

[‡]No data for two patients.

Table 2. Anaphylactic trigger and clinical features of the initial anaphylactic reaction (comparison of biphasic vs. uniphasic episodes)

Description	Biphasic (<i>n</i> = 12)	Uniphasic (<i>n</i> = 95)	<i>P</i> value
Median time to anaphylaxis from exposure (minutes)	10 (2–210)	10 (1–450)	0.62
Type of allergen			
Food (%)	9 (75%)	79 (83%)	0.44
Drug (%)	1 (8%)	7 (7%)	1.0
Insect bite (%)	0 (0%)	4 (4%)	1.0
Unknown (%)	2 (17%)	5 (5%)	0.16
Route of allergen			
Oral (%)	9 (75%)	82 (86%)	0.3
Subcutaneous (%)	0 (0%)	4 (4%)	1.0
i.v. or i.m. (%)	1 (8%)	4 (4%)	0.45
Topical (%)	0 (0%)	1 (1%)	1.0
Unknown (%)	2 (17%)	4 (4%)	0.13
Clinical features			
Respiratory features (%)	11 (92%)	90 (95%)	1.0
URT obstruction (%) [*]	9 (75%)	50 (53%)	0.22
CVS features (%)	4 (33%)	20 (21%)	0.46
Hypotension (%) [†]	3 (38%)	10 (21%)	0.38
GIT features (%)	2 (17%)	90 (95%)	0.17
Skin features (%)	10 (83%)	29 (31%)	0.50

*Upper respiratory obstruction includes tongue swelling, swelling/tightness in throat, stridor, difficulty talking and/or hoarse voice.

[†]BP recorded in only three out of eight biphasic cases and 10 out of 47 uniphasic cases.

i.v., intravenous; i.m., intra-muscular.

Anaphylactic trigger and clinical features of anaphylaxis. There were no significant differences between the groups with respect to the time to anaphylaxis following exposure to the offending agent, the type of anaphylactic trigger, or the route of exposure (Table 2). The specific food trigger did not differ significantly between the two groups (*P* > 0.05 for all comparisons; data not shown). No clinical feature at the initial anaphylactic reaction reliably distinguished uniphasic from biphasic reactors (Table 2).

Therapeutic interventions. Out of the 64 episodes (60 uniphasic and four biphasic reactors) that were treated with parenteral adrenaline alone [Subcutaneous (s.c.) *n* = 34, intravenous (i.v.) *n* = 7 or intramuscular (i.m.) *n* = 23], 15 (23%) episodes required two or more doses of adrenaline (median 2, range 2–3). The rates of second adrenaline administration for the primary anaphylactic reaction were similar for the three modes of parenteral delivery (data not shown; *P* > 0.05 for all comparisons).

Biphasic reactors were significantly more likely to have received, at the time of initial anaphylaxis, > 1 dose of adrenaline (58% vs. 22%, *P* = 0.01), a greater total amount of adrenaline (0.6 vs. 0.1 mg, *P* = 0.047) and/or an i.v. fluid bolus (42% vs. 8%, *P* = 0.01) than uniphasic reactors (Table 3).

Table 3. Therapy administered at initial anaphylaxis (biphasic vs. uniphasic episodes)

Therapy	Biphasic (<i>n</i> = 12)	Uniphasic (<i>n</i> = 95)	<i>P</i> value
<i>Adrenaline</i>			
Administered (%)	9 (75%)	80 (84%)	0.42
Route of administration (%) [*]			
Parenteral alone (s.c., i.v. or i.m.)	4 (44%)	60 (75%)	0.11
Nebulized alone	1 (11%)	5 (6%)	0.48
s.c., i.v. or i.m. plus nebulized	4 (44%)	12 (15%)	0.05
Unknown	0 (0%)	3 (4%)	1.0
Site of initial adrenaline administration [*]			
RCH ED	5 (56%)	38 (48%)	0.73
Local hospital ED	3 (33%)	13 (16%)	0.20
General practitioner's office	1 (11%)	16 (20%)	1.0
Parents	0 (0%)	6 (8%)	1.0
Ambulance	0 (0%)	7 (9%)	1.0
Median time to first dose (min)	28 (3–130)	40 (1–300)	0.7
> 1 adrenaline dose administered at initial anaphylaxis	7 (58%)	21 (22%)	0.01
Median total adrenaline dose (mg/kg) administered at initial anaphylaxis	0.6 (0–3)	0.1 (0–1.4)	0.047
<i>Corticosteroids</i>			
Administered	10 (83%)	75 (79%)	1.0
Median time to first dose (min)	108 (20–260)	90 (17–355)	1.0
Mean dose administered (mg/kg) [†]	0.96 (0.3)	1.1 (0.4)	0.13
<i>Antihistamines</i>			
Administered	8 (67%)	57 (60%)	0.74
Median time to first dose (min)	115 (20–170)	88 (–70–440) [‡]	0.44
<i>Other therapies</i>			
i.v. fluid resuscitation (%)	5 (42%)	8 (8%)	0.01
Median volume (mL/kg) of fluid bolus	20 (8–56)	15 (2–33)	0.46
Oxygen required (%)	6 (50%)	29 (31%)	0.52
Intubated (%)	1 (8%)	0 (0%)	0.13
Salbutamol via spacer/nebulizer (%)	4 (33%)	30 (32%)	1.0
Corticosteroids continued as inpatient (%)	2 (17%)	18 (19%) [§]	1.0
Antihistamines continued as inpatient (%)	0 (0%)	13 (14%) [§]	0.20

Bold was used to highlight which comparisons between the two groups reached statistical significance (i.e. $p < 0.05$).

^{*}Biphasic, $n = 9$; Uniphasic, $n = 80$.

[†]All steroid doses converted to prednisolone equivalent dose (1 mg dexamethasone, 6.67 mg prednisolone; 1 mg methylprednisolone, 1.25 mg prednisolone; 1 mg hydrocortisone, 0.25 mg prednisolone).

[‡]One patient received antihistamines 70 min before anaphylaxis.

[§]Out of 94 episodes (one data point missing).

s.c., subcutaneous; i.v., intravenous; i.m., intramuscular; ED, Emergency Department; RCH, Royal Children's Hospital.

There were no significant differences between the two groups with respect to the route, setting or time to adrenaline administration (Table 3). The number who received

adrenaline via the s.c., i.v. or i.m. route alone did not differ between the two groups (data not shown, $P > 0.05$ for all comparison). Similarly, there were no significant differences between the two groups in the number who received corticosteroids, antihistamines or the total dose of corticosteroid (mg/kg) administered at the time of the initial anaphylactic reaction (Table 3).

The need for > 1 adrenaline dose and/or a fluid bolus during the initial reaction was a sensitive (sensitivity 92%, 95% CI 62–100%) and moderately specific predictor (specificity 76%, 95% CI 66–84%) of a biphasic reaction. The absence of either risk factor was strongly predictive of the absence of a biphasic reaction, with a NPV of 99% (95% CI 93–100%) while the presence of either factor was poorly predictive of a biphasic reaction, with a PPV of 32% (95% CI 17–51%).

Characteristics of biphasic reactions

The characteristics of the 12 biphasic cases are summarized in Table 4. The median time from the onset of the initial anaphylactic reaction to the onset of the biphasic reaction was 8.8 h (1.3–20.5). Out of the 12 biphasic reactions, the second phase was anaphylactic in five (42%), while in the remaining seven (58%), the second phase was non-anaphylactic. Eleven of the 12 children with biphasic reactions (five out of five in whom the second phase was anaphylactic and six out of seven in whom the second phase was non-anaphylactic) received either > 1 dose of adrenaline and/or a fluid bolus during their initial anaphylactic reaction.

Compared with the first anaphylactic episode, the biphasic reaction was milder in seven cases (58%), of similar severity in four cases (33%), and more severe in one case (9%) (Table 4). In 11 of the 12 biphasic cases (92%), repeat therapy (adrenaline, corticosteroids and/or antihistamines) was administered, and one case required an adrenaline infusion for hypotension that occurred 1.5 h after the initial anaphylactic reaction (patient 3; Table 4). Children with biphasic reactions in whom the second phase was anaphylactic in nature tended to be younger (median age 2.0 vs. 13 years, $P = 0.36$) and their time to a rebound reaction shorter (median time 1.5 h vs. 16 h, $P = 0.14$) compared with those children who experienced a non-anaphylactic rebound reaction. These comparisons failed to reach statistical significance.

Discussion

Literature on biphasic reactions following anaphylaxis has focused predominantly on adult presentations [1, 3, 4, 8–10, 16]. Our study examined children presenting with anaphylaxis to a major paediatric ED and found that the severity of the initial anaphylactic reaction, based on the need for > 1 dose of adrenaline and/or an i.v. fluid bolus

Table 4. Characteristics of the children with biphasic reactions (*n* = 12)

No.	Age (years)	Gender	Trigger	Clinical features of initial reaction vs. biphasic reaction*	Severity of biphasic reaction	Time to biphasic reaction (h)	Therapy for initial reaction vs. biphasic reaction†
1	0.2	F	Food (cow's milk)	U, S, T	Similar	1.2	A
2	0.4	M	Food (egg)	A, Co, H, S, U, V, W	Milder	6.5	A, S, O, F
3	1.5	M	Food (soy milk)	Co, S, T, U, W	More severe	1.5	A, S, O
4	2	M	Food (cashew)	Co, T, U, W	Similar	1.4	A, AH, S, F
5	7.7	M	Food (tuna) and exercise	V, D, ICS	Milder	20.5	F
6	14.8	M	Food (prawn)	A, DS, S, U	Milder	3.2	A, AH, S
7	2.9	F	Food multiple (egg, treenut, peanut)	A, S, TS, U	Milder	3.0	A, AH, S
8	11.6	M	Food multiple (pizza, ice-cream with nuts)	A, DS, S, T	Similar	13.8	A, AH, S, O
9	16.7	F	Food multiple (fish and pistachios)	A, DS, H, S, T, TS, U	Milder	18.0	AH, S, F
10	15.3	M	Drug (Penicillin)	C, Co, H, T, W	Similar	11.1	A, AH, S, F, O
11	12.9	F	Unknown	DS, T, U, W	Milder	16.0	A, AH, S, O
12	13.7	M	Unknown	A, DS, T, U	Milder	17.5	AH, S, O

*A, angioedema; C, cyanosis; Co, cough; D, diarrhea; DS, difficulty swallowing; H, hypotension; HV, hoarse voice; ICS, impaired conscious state; S, stridor; T, tachypnea; TS, tongue swelling; U, urticaria; V, vomiting; W, wheeze.

†A, adrenaline; AH, anti-histamines; AI, adrenaline infusion; F, fluids; O, oxygen.

at presentation, to be associated with an increased risk of a biphasic reaction. The absence of either of these markers was strongly predictive of the absence of a biphasic reaction. These findings have not been previously reported in children.

In the only other paediatric study of biphasic reactions, Lee and Greenes [2] reported a biphasic rate of 6%, in which all second phase reactions were anaphylactic in nature. We found a higher rate of biphasic reactions (11%), although the rate of second phase anaphylactic reactions (5/109, 5%) was similar to that reported by Lee and Greenes [2]. In keeping with other reports in adults [8], the majority of biphasic reactions (91%) in our study appeared to be either milder or of similar severity to the original presentation. Unlike Ellis and Day [8], we found urticaria to be as common during the primary anaphylactic event ($n = 9/12$), as compared with the biphasic phase ($n = 10/12$).

Lee and Greenes [2] found a delay in the administration of adrenaline during the initial anaphylactic reaction to be associated with a biphasic response in children. Several studies examining predictors for biphasic anaphylaxis in adults or mixed adult-paediatric populations, with the latter only including a small number of children, identified the need for a large dose of adrenaline at primary anaphylaxis [16], an inadequate amount of adrenaline and a slow time to resolution of the initial anaphylactic reaction [8], oral route of antigen exposure [6], slow onset of initial anaphylactic symptoms and the presence of less frequent and less severe respiratory features at the time of anaphylaxis [5] to be associated with a biphasic response. Douglas *et al.* [1] did not report any factor that could reliably predict a biphasic response, however, examination of their data reveals that biphasic reactors received fluid boluses more often at the initial anaphylactic reaction, compared with uniphasic reactors ($n = 2/4$, 50% vs. 4/56, 7%; $P = 0.046$).

Consistent with the studies of Brazil and MacNamara [16] and Douglas *et al.* [1], we also identified an increased requirement for adrenaline and/or fluid bolus to be associated with a biphasic response, but failed to confirm other previously identified risk factors. It is interesting to note that in our series, the administration of fluid resuscitation in an individual did not track with the volume of fluid bolus administered or the presence of hypotension, and that it was the decision to initiate fluid resuscitation rather than the volume of fluid administered or the presence of hypotension that was a risk factor for biphasic anaphylaxis.

No study to date has found a prior history of anaphylaxis, the presence of asthma or specific allergen triggers to predispose to biphasic reactions. Some have suggested that biphasic reactions rarely occur without hypotension or upper respiratory tract obstruction during the initial anaphylactic episode [17]. However, in all studies, the presence of these clinical features was not able to reliably

predict biphasic reactors [1, 5, 6, 16]. Taken together, interpretation of current evidence suggests that the severity of the initial anaphylactic event and/or its inadequate treatment with adrenaline are risk factors for a biphasic reaction. In our series, 18 children who initially presented with clear features of anaphylaxis, some with impaired consciousness and hypotension, failed to receive any form of adrenaline, highlighting the often inadequate treatment of anaphylaxis, even in the setting of a tertiary level paediatric emergency department.

Corticosteroid administration is often recommended as part of anaphylaxis management, with some suggesting this may suppress biphasic reactions [1, 8]. We, like others, did not find that the rate of corticosteroid or antihistamine use during the initial anaphylactic reaction was significantly different between patients with uniphasic vs. biphasic reactions [1, 2, 4, 6, 8, 16]. Furthermore, in our study, the number of children receiving regular administration of corticosteroids or antihistamines following anaphylaxis was not significantly different between uniphasic vs. biphasic reactors. Although administration of corticosteroids and antihistamines may be beneficial in some individuals [9], of more importance is ensuring all patients presenting with anaphylaxis receive a prompt and adequate dose of adrenaline.

One of the main reasons for admission once a child has been stabilized following anaphylaxis is to monitor for a biphasic reaction and administer treatment when required. Our overnight admission rate into hospital was 62% ($n = 90/145$), but only seven of the 109 included cases (6%) had serious rebound ($n = 5$) or protracted ($n = 2$) reactions that benefited from an inpatient stay, as defined by the need for emergency medical treatment. Lee and Greenes [2] found only 2% of anaphylactic episodes had biphasic reactions that benefited from admission. The period of observation required post-anaphylaxis is difficult to gauge given the wide-range of time intervals observed between the initial and biphasic reaction, with some biphasic reactions occurring 24 h after the initial reaction [9]. Although a prospective trial is required to confirm whether the risk factors found in this study could reliably and safely be used to decide who may benefit from prolonged observation, our findings suggest that children presenting with anaphylaxis who do not receive > 1 dose of adrenaline or a fluid bolus, are at low risk for developing a biphasic reaction, whereas those who receive > 1 dose of adrenaline and fluid resuscitation should be observed for 24 h. Because no risk factor to date, including the ones identified in this study, would be able to capture all patients at risk of a biphasic reaction, clinicians must ensure that any patient discharged from hospital following anaphylaxis has an emergency plan in place and injectable adrenaline available to ensure adequate management of any subsequent biphasic reaction.

The limitations of this study include its retrospective design and the inability to measure biphasic reactions in non-hospitalized individuals. Inherent to any retrospective analysis is the potential for inadequate or incomplete documentation. However, our retrospective design is unlikely to have affected the measurement of our primary outcome (the rate of biphasic reaction) because the need for any subsequent medical therapy is always documented in the patient's drug chart and nursing notes. We believe the rate of the biphasic reaction reported in this study is accurate, and indeed, our prevalence of biphasic reactions in which the second phase was anaphylactic is similar to that reported by the only other paediatric study of biphasic reactions [2]. We were unable to determine the rate of biphasic reaction in children who were directly discharged from the ED. However, this particular group of children did not live far from medical services, with 78% living within zones 1 and 2 as defined by the Melbourne Metropolitan Train Service (maximum distance to the central business district of 20 km), so that if a second anaphylactic reaction had occurred, one would have expected re-presentation of at least some of these children back to our ED.

In conclusion, biphasic reactions in our series occurred in 11% of children, almost half of whom (5%) had a more serious biphasic anaphylactic reaction. Biphasic reactions were unlikely in those receiving only a single dose of adrenaline and/or no fluid bolus at the time of the initial anaphylaxis. Children receiving >1 dose of adrenaline and/or a fluid bolus should be observed in hospital for 24 h.

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