ORIGINAL ARTICLE

Proposed use of adrenaline (epinephrine) in anaphylaxis and related conditions: a study of senior house officers starting accident and emergency posts

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Submitted 17 December 2001
Accepted 4 March 2002

Postgrad Med J 2002;**78**:416–418

Senior house officers (SHOs) (n=78) at the start of their accident and emergency (A&E) post were given an anonymous five case history questionnaire, containing one case of true anaphylaxis, and asked to complete the medication they would prescribe. In the case of anaphylaxis, 100% would administer adrenaline (epinephrine) but 55% would do so by the incorrect route. In the remaining cases, 10%–56% would be prepared to administer adrenaline inappropriately. Only 5% were able to indicate the correct route and dose of adrenaline according to Resuscitation Council guidelines (UK). This has implications for training as the survey took place before the start of the A&E posting. Anaphylaxis is over-diagnosed and poorly treated despite Resuscitation Council guidelines.

Anaphylaxis describes a severe systemic allergic response in which respiratory difficulty and/or hypotension is *invariably* present.[1] In addition there are likely to be a number of other clinical features which are *variably* present (table 1). Anaphylaxis is typically a type I hypersensitivity reaction, leading to sudden mast cell and basophil degranulation, mediated by IgE. Cardiovascular collapse is caused by vasodilatation and increased vascular permeability. Respiratory difficulty may be due to laryngeal oedema or bronchospasm. The most common precipitants include insect stings, drugs or contrast media, and certain foods. In each case, a thorough history and clinical examination should be performed to assess the presence and severity of the allergic features, and to reach the correct diagnosis.

Any of the constellation of features included in an anaphylactic reaction can have a multitude of causes, which may be misinterpreted as an "allergic" reaction. Symptoms or clinical signs such as urticaria or angioedema may be classified and treated as "anaphylactic", even in the absence of cardiovascular or respiratory compromise. Anaphylactic reactions can also vary in severity and progress may be rapid, slow, or (unusually) biphasic.[2]

Table 1 Typical clinical features of anaphylaxis. One or more features in the left hand box are invariably present, in association with a combination of features in the right hand box

Laryngeal oedema	Colour change: flushed or pale
Bronchospasm	Erythema
Fainting and lightheadedness	Pruritis (generalised)
Cardiovascular collapse	Urticaria
Loss of consciousness	Angioedema
	Rhinitis
	Conjunctivitis
	Itching of palate or external auditory meatus
	Nausea
	Vomiting
	Abdominal pain
	Palpitations

METHODS

Case histories based on five patients referred to an immunology clinic, after an acute presentation to the accident and emergency (A&E) department, were summarised. These were used in a questionnaire, given to 78 senior house officers (SHOs) attending an induction day before the start of their posting in A&E medicine in the Southwest region. A uniform answer box, including the choices of adrenaline (epinephrine) available in the A&E department, was given for each of the five questions. Respondents were then requested to circle appropriate treatments in an answer square for each scenario. The questionnaire was completed anonymously and subjects were informed they were completing this as a part of a study. There was no compulsion to participate. There was no teaching on the subject during the induction course.

Cases

1. A 55 year old woman is admitted by ambulance with a widespread, raised erythematous rash immediately after eating shellfish. She is acutely dyspnoeic, wheezing, and hoarse. She is conscious. Intravenous access is established. Her pulse is 110 beats/min, blood pressure 80/60 mm Hg, respiratory rate 28/min, oxygen saturations 90% on oxygen.

2. A 32 year old man presents with dyspnoea 15 minutes after eating two packets of dry salted peanuts. He doesn't have a rash. He has difficulty talking and complains that his throat feels swollen. He has inspiratory stridor but no wheeze. His pulse is 90 beats/min, blood pressure 145/78 mm Hg, respiratory rate 24/min, oxygen saturations 98% on air.

3. A 30 year old man has a widespread, pruritic, raised erythematous rash developing over 45 minutes. He carries an Epipen (Meridian Medical Technologies, Columbia, MD, USA) prescribed by his general practitioner for previous similar occurrences and has used this before arrival. He has no wheeze. His pulse is 110 beats/min, blood pressure 158/96 mmHg, respiratory rate 18/min, oxygen saturations 100% on air.

Abbreviations: A&E, accident and emergency; SHO, senior house officer

Box 1: Resuscitation Council guidelines for anaphylactic reactions: treatment of adults by first medical responders[1 3]

Anaphylaxis should be considered:

When there is a history compatible with severe allergic reaction including respiratory difficulty and/or hypotension, especially with typical skin changes present (urticaria and/or angioedema).
If the patient is assessed and there is STRIDOR, WHEEZE, and clinical signs of SHOCK:

- Adrenaline should be administered 0.5 ml 1/1000 solution (500 µg) intramuscularly, which may be repeated after five minutes.

Other treatments:

- Antihistamine (chlorpheniramine) 10–20 mg intramuscularly/or slow intravenously
- Hydrocortisone 100–500 mg intramuscularly/or slowly intravenously: for all severe or recurrent reactions and patients with asthma.
- If clinical manifestations of shock do not respond to drug treatment give 1–2 litres intravenous fluid.

Other notes:

1. An inhaled β_2-agonist such as salbutamol may be used as an adjunctive measure if bronchospasm is severe and does not respond rapidly to other treatment.
2. If profound shock is judged immediately life threatening give cardiopulmonary resuscitation/advanced life support as necessary. Consider slow intravenous adrenaline (epinephrine) 1:10 000 solution. This is hazardous and is recommended only for an experienced practitioner who can also obtain intravenous access without delay. Note the different strength of adrenaline (epinephrine) that may be required for intravenous use.
3. If adults are treated with an Epipen, the 300 µg will usually be sufficient. A second dose may be required.
4. Half doses of adrenaline (epinephrine) may be safer for patients on amitriptyline or imipramine, intravenous salbutamol may be required for patients on a β-blocker.
5. A crystalloid may be safer than a colloid.

4. A 26 year old woman has a widespread, erythematous rash and puritis one day after starting a course of penicillin for an upper respiratory tract infection. She has a history of asthma and of a previous rash with antibiotics but doesn't know which. Her pulse is 104 beats/min, blood pressure 97/55 mm Hg, respiratory rate 16/min, oxygen saturations 98% on air, peak flow rate 80% of that predicted.

5. A 74 year old man has a grossly swollen lower lip and tongue swelling developing over the last 45 minutes. His history includes ischaemic heart disease and hypertension. He has difficulty talking because of the tongue. He has no audible stridor or wheeze. His pulse is 84 beats/min, blood pressure 168/95 mm Hg, respiratory rate 18/min, oxygen saturations 97% on air.

RESULTS

The replies have been collated to provide the following data for each case, 1–5:

- The percentage of the total group of respondents electing to use adrenaline.
- The percentage of the total group of respondents electing to use each route of administration for adrenaline, namely intramuscular, intravenous, or subcutaneous.
- The percentage of those using intramuscular adrenaline that chose the dose recommended by the Resuscitation Council guidelines[1 3] for the treatment of anaphylaxis (0.5 mg or 0.5 ml of 1 in 1000) (box 1).

The respondents were not asked what they thought the diagnosis was for each case. The diagnosis given in the table below (table 2) reflects the final diagnosis for each patient as made when they were reviewed in the immunology clinic after their acute presentation.

These results demonstrate that although all the SHOs treated the case of anaphylaxis (case 1) with adrenaline, there was considerable confusion regarding the correct route and dose of administration. Forty two per cent of the group elected to use intravenous adrenaline, and of those using the recommended intramuscular route, only 20% used the recommended dose. Out of the total group of 78 respondents, only 5% administered adrenaline in accordance with the Resuscitation Council guidelines for the management of acute anaphylaxis.

Cases 2–4 are not characteristic of acute anaphylaxis, they do not have the potentially life threatening features present.[4 5] However some of the SHOs opted to use adrenaline, with a significant number choosing intravenous bolus doses as used in cardiac arrest protocols.

DISCUSSION

The correct diagnosis and treatment of anaphylaxis can be life saving.[1] Ewan suggests the diagnosis be reserved for life threatening features—namely, respiratory difficulty (laryngeal oedema or bronchoconstriction), hypotension, and/or collapse.[4] Using these criteria, only case 1 would be classified as acute anaphylaxis.

There are a wide range of possible clinical manifestations of acute anaphylaxis, many of which overlap with features seen in less severe allergic reactions or other medical conditions. The potential for misdiagnosis by relatively junior medical staff was recognised by the authors of the Resuscitation Council guidelines.[1 3] For this reason they emphasised the importance that the first line treatment for anaphylaxis should be safe even in inexperienced hands. Establishing a gold standard for the management of anaphylaxis is difficult.

Table 2 Analysis of results; percentages are of total respondents (n = 78)

Case No	Diagnosis	Adrenaline given: all routes + all doses*	Intramuscular adrenaline: any dose	Intramuscular adrenaline (0.5 mg): any concentration†	Intravenous adrenaline: any dose	Subcutaneous adrenaline: any dose
1	Anaphylaxis	78 (100)	35 (45)	10 (13)	33 (42)	6 (8)
2	Foreign body inhalation (confirmed negative by skin prick test and oral challenge)	44 (56)	23 (29)	6 (8)	13 (17)	3 (4)
3	Urticaria	8 (10)	3 (4)	3 (4)	1 (1)	2 (3)
4	Rash, ?antibiotic related, mild exacerbation of asthma	17 (22)	6 (8)	5 (6)	5 (6)	2 (3)
5	Angioedema (with ischaemic heart disease)	32 (41)	17 (22)	6 (8)	7 (9)	5 (8)

*Including those where the route of administration was omitted.
†Irrespective of the concentration selected: either 1/1000 or 1/10000 solution.

Randomised treatment trials are impractical. Current guidelines recommend adrenaline be used by the intramuscular route and that intravenous adrenaline should only be administered in cases of life threatening anaphylaxis, by experienced clinicians, not SHOs, and with adequate monitoring.

Our findings suggest that in this group of respondents there was a tendency to over-diagnose anaphylaxis, resulting in the over use of adrenaline. This contrasts with a retrospective study done in 1993–94 which concluded that there was a reluctance by A&E staff to use adrenaline.[4] Guidelines are of use only if the diagnosis is correct. Our cohort had not received formal teaching on anaphylaxis management and we suggest that improved training in this area is required.

Serum mast cell tryptase levels are raised in the first 1–2 hours after mast cell activation, with a half life of approximately two hours. Raised levels are therefore seen in the context of anaphylaxis and are stable even in serum samples stored at room temperature. Measurement of mast cell tryptase can be helpful in confirming anaphylaxis and anaphylactoid reactions.[6 7] Any patient with a severe reaction should be referred to an allergy clinic so that the potential cause may be determined and avoided in future. Patients with positive histories and other supportive evidence such as positive allergen testing may be given advice on the self treatment with adrenaline using preloaded syringes such as the Epipen.

This study highlights the confusion regarding the correct dose, concentration, and route of administration for adrenaline recommended in the treatment of anaphylaxis. Treatment with intravenous or excess adrenaline can be dangerous.[8]

FURTHER LINKS

http://www.resus.org.uk

ACKNOWLEDGEMENTS

We thank Dr Rupert Evans, Emergency Unit, University Hospital of Wales for advice and coordination of the questionnaire and Mr R L Baird for help with database formation.

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