

Review article

Comparison of international guidelines for the emergency medical management of anaphylaxis

Background: Guideline-based treatment approaches for managing anaphylaxis are widely believed to result in good outcomes, but the strength of evidence underpinning the recommendations made therein is unclear.

Objective: To identify and compare national guidelines for the emergency medical management of anaphylaxis and to describe the extent to which the evidence base in support of key recommendations is made clear.

Methods: We systematically searched key medical databases and contacted the World Allergy Organization and anaphylaxis charities in several countries to identify national guidelines. Full text copies of relevant papers were obtained and, where necessary, translated. Data were abstracted onto a customized data extraction sheet; this process was independently checked by a second reviewer.

Results: Guidelines originating from Australia, Canada, Russia, UK, Ukraine and the USA were identified. While these were in agreement on the broad principles of management, there were important variations in relation to the treatments to be used and the dose and route of administration of these preparations. Most guidelines failed to make clear the strength of evidence underpinning the recommendations being made.

Conclusions: There are important international differences in the recommended emergency management of anaphylaxis. It is important that an agreed core evidence-based guideline for the management of anaphylaxis is now developed, which can then be adapted for national/local use. Clinicians need to be aware of the limitations of existing guidelines.

M. Alrasbi, A. Sheikh

Allergy & Respiratory Research Group, Division of
Community Health Sciences, University of
Edinburgh, Edinburgh, UK

Key words: anaphylaxis; emergency; evidence-based;
guidelines; international.

Aziz Sheikh
Allergy & Respiratory Research Group
Division of Community Health Sciences
University of Edinburgh
20 West Richmond St
Edinburgh EH8 9DX
UK

Accepted for publication 23 April 2007

Anaphylaxis is a medical emergency that is responsible for considerable morbidity and, in some cases, mortality, much of which may be potentially avoidable (1). There have however been several important barriers to establishing the evidence base needed to develop scientifically sound management pathways, these including the lack of a universally acceptable definition, a pathophysiologically helpful, but clinically cumbersome classification system, and the ethical and logistical difficulties in mounting prospective epidemiological studies and clinical trials of treatments commonly used (2).

But despite these barriers, there has recently been some welcome progress in moving towards a consensus clinical definition for anaphylaxis (3), the development of the World Allergy Organization's proposed revised classification system for anaphylaxis (4), and the potential offered for epidemiological studies by the increasing numbers of large national datasets (5). While these developments are welcome, the focus of the evidence-based movement remains very much on assessing the strength of evidence underpinning therapeutic interventions, as it is here that there is the greatest risk of iatrogenic harm (6).

As a key step in our on-going work to make explicit the evidence base underpinning the management of anaphylaxis, we sought to identify and compare the recommendations made in key national guidelines for the emergency medical management of anaphylaxis and assess the extent to which, if any, these made clear the strength of evidence underpinning the various recommendations made.

Methods

We used several approaches to identify current guidelines for the emergency management of anaphylaxis. This included drawing on our own database of anaphylaxis publications, searching The National Guideline Clearinghouse, which is an online database of international evidence-based clinical practice guidelines maintained by the US Agency for Healthcare Research and Quality (7), PubMed database and the Internet through the Google search engine. Appropriate search strategies were constructed depending on the databases being searched (further details are available on request from the last author). In addition, we wrote to the World Allergy

Table 1. Summary of recommendations in key international guidelines for the emergency medical management of anaphylaxis

Country, year of publication, reference	Posture	Oxygen	Adrenaline	Antihistamines	Steroids
Australia, 2006 (9)	Supine (or left lateral if vomiting); elevate legs if tolerated	High flow	1 : 1000 solution 0.01 mg/kg (max. 0.5 mg); I.m. (lateral thigh)	Not recommended	Not recommended
<i>Strength of evidence</i>	Level I.v. i.e. case series	Not mentioned	Giving adrenaline is level I.v. i.e. case series; site of administration is level I.v. i.e. well designed pseudo-randomized controlled trials	N/A	N/A
Canada, 2003 (10)	Not mentioned	Supplemental O ₂	1 : 1000 solution I.m. child 0.01 ml/kg max. 0.3 ml Adult 0.3–0.5 ml	Diphenhydramine I.v. i.m. or p.o. Adults: 25–50 mg Child: 1.25 mg/kg + Ranitidine I.v. or p.o. Adults: 50 mg i.v. or 150 mg p.o. Child: 1.25 mg/kg i.v. or 2 mg/kg p.o.	Methylprednisolone I.v. or Prednisone P.o. Adults: 125 mg i.v. or 50 mg p.o. Child: 1 mg/kg i.v. or 1 mg/kg p.o.
<i>Strength of evidence</i> Russia, 2004 (11)	N/A Supine position Lift the chin upwards and turn the head to the left side	Not mentioned Supplemental O ₂ + ethanol as an antifoam agent	Not mentioned 1 : 1000 solution S.c. or i.m. adults: 0.3–0.5 ml (0.3–0.5 mg) Child: 0.01 mg/kg	Not mentioned Diphenhydramine Adults: 25–50 mg Child: 1–2 mg/kg I.v. or i.m. Promethazine 2.5% – 2–4 ml i.v. or i.m. chlorphenamine 2% – 2–4 ml i.v. or i.m. Expert opinion Chlorphenamine >12 years 10–20 mg i.m. or slow I.v. 6–12 years 5–10 mg i.m. 1–6 years 2.5–5 mg i.m.	Not mentioned Prednisolone 1–2 mg/kg I.v. Hydrocortisone 100–300 mg i.m. or I.v. Dexametasone 4–20 mg i.v.
<i>Strength of evidence</i> UK, 1999 (revised 2002 & 2005) (12)	Not mentioned Lie flat with legs raised (unless respiratory distress increased)	Not mentioned High flow O ₂ (10–15 l/min)	Not mentioned 1 : 1000 solution Adults: 0.5 ml (0.5 mg) i.m. children > 12 years up to 0.5 mg i.m. 6–12 years 0.25 I.m. > 6 month–6 years 0.12 mg I.m. < 6 month 0.05 mg i.m.	Not mentioned Hydrocortisone 12 years >100–500 mg i.m. or slow I.v. 6–12 years 100 mg i.m. 1–6 years 50 mg i.m.	Not mentioned Hydrocortisone 12 years >100–500 mg i.m. or slow I.v. 6–12 years 100 mg i.m. 1–6 years 50 mg i.m.
<i>Strength of evidence</i>	General statement that no definitive trials exist and that recommendations are consensus-based.				
Ukraine, 2002 (13)	Supine position	Supplemental O ₂ + ethanol as an antifoam agent	1 : 1000 solution S.c. or i.m. adults: 0.3–0.5 ml (0.3–0.5 mg) child: 0.01 mg/kg	Diphenhydramine Adults 25–50 mg Child: 1–2 mg/kg I.v. or i.m. Promethazine 2.5% – 2–4 ml i.v. or i.m.	Prednisolone 1–2 mg/kg I.v. Hydrocortisone 100–300 mg i.m. or I.v. dexametasone 4–20 mg i.v.

Table 1. (Continued)

Country, year of publication, reference	Posture	Oxygen	Adrenaline	Antihistamines	Steroids
<i>Strength of evidence</i> USA, 2005 (14)	Not mentioned Recumbent position and elevate lower extremities	Not mentioned 6–8 l/min guided by arterial blood gasses or oxymetry	Not mentioned 1 : 1000 solution 0.2–0.5 ml (0.01 mg/kg in children, maximum 0.3 mg) i.m. or S.c. lateral thigh	Not mentioned Diphenhydramine Adults 25–50 mg i.v. child 1 mg/kg up to 50 mg. Oral might be sufficient for milder attacks + ranitidine Adults: 1 mg/kg Child: 12.5–50 mg infused over 10–15 min Not mentioned, although stated that no data from controlled studies	Not mentioned Not recommended for use as part of acute management.
<i>Strength of evidence</i>	Not mentioned	Level A/D i.e. evidence from expert opinion/clinical experience or extrapolated from higher order evidence	Level A/D i.e. evidence from expert opinion/clinical experience or extrapolated from higher order evidence		N/A

Organization and anaphylaxis support organizations in the US, Canada, the Netherlands, Germany, Italy, Australia, New Zealand and Japan through the UK-based Anaphylaxis Campaign to ascertain if they were aware of any guidelines being used in their own countries.

All searches were conducted in the period June–September 2006. Where necessary, relevant sections from guidelines were translated into English. In the event of finding more than one guideline in different countries we focused on the more widely known and/or recent version.

Data were abstracted onto a customized data extraction sheet by one researcher and this process was checked by the second researcher. For each country, we assessed the extent to which the evidence base underpinning the recommendations was made explicit using established criteria and assessed for areas of convergence and divergence between recommendations being made in different guidelines (8).

Results

We were able to identify current guidelines for the emergency medical management of anaphylaxis for Australia, Canada, Russia, UK, Ukraine and the USA (9–14). Table 1 details the key recommendations made in each of these guidelines and also makes clear whether or not the evidence underpinning these recommendations is made clear in the respective guidelines.

As is clear from inspecting the table, while all agree on the central role of adrenaline, there is however, no clear agreement on the role of other commonly used first-line approaches and agents. There are thus important differences in recommendations regarding posture, use of adrenaline, corticosteroids, H1- and H2-antihistamines, oxygen and bronchodilators.

Discussion

We have found important variations in recommendations for the management of acute anaphylaxis, this to a large extent reflecting the poorly developed underlying scientific base. Furthermore, the lack of clarity of the strength of evidence underpinning many of these recommendations suggests that most are likely to be influenced by the particular experiences and perspectives of key individuals within guideline committees. Although the possible influence of the pharmaceutical industry cannot be excluded, given the fact that in the main generic treatments are being recommended, it is unlikely that industry will have exerted much of an influence.

Strengths and limitations of this work

The main strengths of this work include the attempt to locate relevant guidelines through a number of routes

which ultimately resulted in identifying guidelines from countries in three continents, the *a priori* agreed evaluation criteria (8), and the standardized approach used to extract and compare data.

Possible limitations include the fact that we may have failed to identify some important guidelines, although, that said, those identified were still sufficient to illustrate the main objectives of this study. Also of relevance is that we made no attempt to assess the extent to which these guidelines are actually followed by clinicians; it may thus be that these are largely ignored in practice and that the actual emergency management approaches used in different parts of the world are more similar than our findings actually suggest. However, anecdotal evidence from the UK suggests that the converse is more likely to be true, with considerable variation in practice even in relation to the recommendation on adrenaline use, which all guidelines agree upon.

Implications of this work

All guidelines for the emergency management of anaphylaxis should make much more explicit the evidence in

support of the various recommendations being made. Furthermore, they should also follow other best practice considerations known to be important in guideline development, these including the need to make clear how any potential conflict of interests were handled and also to set review dates for guideline updates (15).

In an international age with ready opportunity for sharing information globally there is also a need, in the longer term, for a generic international core guideline to be developed, which can then be locally adapted according to needs and circumstances. In the interim, clinicians and their national bodies would do well to study carefully the existing range of guidelines and see if their practice and policies need to be adapted.

Acknowledgments

Our thanks to the World Allergy Organization and David Reading from Anaphylaxis UK in helping to identify relevant guidelines. We would also like to record our appreciation to Dr Ulugbeck Behdiyuruz for his help in translating documents.

References

1. Simons FE. Anaphylaxis, killer allergy: long-term management in the community. *J Allergy Clin Immunol* 2006;**117**:367–377.
2. Walker S, Sheikh A. Managing anaphylaxis: effective emergency and long-term care are necessary. *Clin Exp Allergy* 2003;**33**:1015–1018.
3. Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF, Bock SA, Branum A et al. Second symposium on the definition and management of anaphylaxis: summary report. Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006;**117**:391–397.
4. Johansson SG, Bieber T, Dahl R, Freidmann PS, Lanier BQ, Lockey RF et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol* 2004;**113**:832–836.
5. Anandan C, Simpson CR, Fischbacher C, Sheikh A. Exploiting the potential of routine data to better understand the disease burden posed by allergic disorders. *Clin Exp Allergy* 2006;**36**:866–871.
6. Cochrane AL. Effectiveness and efficiency. Random reflections on health services. London: RSM, 2004.
7. Agency for Healthcare Research and Quality: National Guideline Clearinghouse. <http://www.guideline.gov/>; accessed 3 April 2007.
8. Higgins JPT, Green S (editors). *Cochrane Handbook for systematic reviews of interventions* 4.2.5 (updated May 2005). The Cochrane Library, Issue 3. Chichester: John Wiley, 2005.
9. Brown SGA, Mullins RJ, Gold MS. Anaphylaxis: diagnosis and management. *MJA* 2006;**185**:283–289.
10. Ellis AK, Day JH. Diagnosis and management of anaphylaxis. *CMAJ* 2003;**169**:307–312.
11. Dadikina AB, Duhanina IB, Namazova LC, Vertkin AL, Turlubekov KK. Pre-hospital management in acute allergic reactions: theory and practice. National scientific practice society of emergency medicine. Guidelines for immediate management of anaphylactic reactions. <http://www.doktor.ru>, 2004; accessed 17 May 2007.
12. Resuscitation Council (UK). The emergency medical treatment of anaphylactic reactions for first medical responders and for community nurses. <http://www.resus.org.uk/pages/reaction.htm>, 2005; accessed 3 April 2007.
13. Soloshenko EH. Drug induced anaphylaxis shock. *Medicus Amicus* 2002;**1**:8–9.
14. Lieberman P, Kemp SF, Oppenheimer J et al. (editors). The diagnosis and management of anaphylaxis: an updated practice parameter. *J Allergy Clin Immunol* 2005;**115**:S483–S523.
15. Scottish Intercollegiate Guidelines Network. SIGN 50: A guideline developers' handbook. <http://www.sign.ac.uk/guidelines/fulltext/50/index.html>; accessed 3 April 2007.