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Anaphylaxis diagnostic criteria and management guidelines for the pre-hospital setting: A comparison

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Literature review

Anaphylaxis diagnostic criteria and management guidelines for the pre-hospital setting: A comparison

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Abstract

Introduction

Anaphylaxis is a potentially life-threatening medical emergency and a challenge for emergency healthcare providers. There appears to be a lack of consistency in the international definition and management of anaphylaxis. The objective of this study was to review current international guidelines in diagnostic and management of anaphylaxis in the pre-hospital setting.

Methods

A literature search was conducted of the medical related electronic databases, Ovid MEDLINE, Cinahl, Cochrane CENTRAL and EMBASE from 1980 to the end of May 2013. A previously published pre-hospital search filter was used in each of the databases including additional keywords, 'anaphylaxis', 'diagnosis', 'hypersensitivity', 'allergy', 'allergic reaction', 'adrenaline', 'epinephrine' and 'antihistamine'. Articles were included if their primary aim was to report of the evidence used to create international guidelines of anaphylaxis diagnosis and management. The references of retrieved articles were also reviewed. Articles were excluded if they were not written in English.

Results

There were 128 articles located by the search with 18 meeting the inclusion criteria. Of these, three were literature reviews and six reported on the introduction of anaphylaxis guidelines, including medical treatment in different countries. Three retrospective studies evaluated the efficiency of current diagnostic and management in hospital setting. Two questionnaire surveys were conducted internationally. There were two articles proposing diagnostic criteria and a rating method for anaphylaxis. Two were relevant to pre-hospital studies.

Conclusion

The inconsistency of definition and diagnosis criteria increases the risk of under-diagnosis and under-treatment of patients with anaphylaxis. Emergency healthcare providers need a more explicit set of diagnosis criteria and guidelines for treatment to rapidly relieve patients' anaphylactic reaction and potentially life-threatening situation.

Keywords

emergency medical systems; pre-hospital; anaphylaxis; anaphylaxis guidelines; adrenaline epinephrine

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Introduction

Anaphylaxis is a potentially life-threatening medical emergency (1-3). Triggers, such as bee stings, nuts, certain foods, antibiotics and anaesthetic drugs can cause a wide range of anaphylactic reactions in humans (3,4). An international epidemiology study shows that the incidence rate of anaphylactic episodes lies between 30 and 950 cases per 100 000 persons per year (5). In a pre-hospital anaphylaxis database in the United States of America (USA) the proportion of emergency medical services involvement in suspected allergic reaction or anaphylaxis calls is approximately 0.4–0.9% of all emergency medical services calls (1). There are approximately 20 anaphylaxis deaths each year in the United Kingdom (UK) with the number of individuals suffering from recurrent anaphylaxis estimated at one in 12 per year (4). While the evidence shows that occurrence of anaphylaxis is uncommon, the multiple body systems involved in an anaphylactic reaction might be fatal for some individuals (4). In Australia, the hospitalisation of patients with anaphylaxis has increased significantly from 1993–1994 compared to 2003–2004 (6) with a large majority of these patients treated in the hospital emergency department (ED) (7,8). The death rate from anaphylaxis in the corresponding period has increased from 10 per year in the period 1993–2001 to 20 per year since 2002 (6).

The definition of anaphylaxis varies internationally (1,3,4,9). For instance, the World Allergy Organization (WAO) anaphylaxis guidelines define this condition as ‘a serious, life-threatening generalised or systemic hypersensitivity reaction’ and ‘a serious allergic reaction that is rapid in onset and might cause death’ (3). In contrast, the Canadian Paediatric Surveillance Program defines anaphylaxis as ‘a severe allergic reaction to any stimulus, having sudden onset and generally lasting less than 24 hours, involving one or more body systems and producing one or more symptoms such as hives, flushing, itching, angioedema, stridor, wheezing, shortness of breath, vomiting, diarrhoea or shock’ (1). One of the major challenges of managing anaphylaxis faced by clinicians is that there is neither a universally accepted definition nor a set of standardised diagnosis criteria internationally. Therefore, the potential risk for an individual is that anaphylaxis could be under-recognised and under-treated by emergency healthcare personnel (1).

There are many medications used to revert and/or reduce an anaphylactic reaction (1,10-12). One, adrenaline, is used as the first line medication for treatment of anaphylaxis (1,13). However, several studies indicate that adrenaline and other drugs used for allergic reactions, such as antihistamines and corticosteroids, have not yet had validated prospective, randomised controlled trials on emergency patients who present with an anaphylactic reaction (1,14-16). Studies also indicate that there is no standardised treatment for anaphylactic patients internationally (1,11,12,17).

Due to the inconsistency of definition and diagnostic criteria for anaphylaxis, it is difficult for emergency healthcare providers to diagnose and manage patients with potentially life-threatening anaphylactic reactions (1). The aim of this study was to review current international guidelines in diagnostic and management of anaphylaxis in the pre-hospital setting.

Methods

A literature search of related electronic medical databases was undertaken by using the Ovid and EBSCOhost systems available through the Monash University library in Melbourne, Victoria. The online databases searched included the Cochrane Library, MEDLINE, and CINAHL from 1993 to 2013. The MeSH headings and keywords used for the search were: ambulance, emergency medical services, paramedics, emergency medical technician, EMT, out-of-hospital, out of hospital, pre-hospital, anaphylaxis, anaphylactic reaction, anaphylaxis guidelines, anaphylaxis criteria, anaphylaxis diagnosis, hypersensitivity, allergy, allergic reaction, adrenaline, epinephrine, antihistamine. The MeSH headings and keywords were used individually and in combination during the search process. The duplicated and non-English articles were removed from the result lists. Reference lists of identified articles were reviewed, and a hand search of relevant published literature performed.

Articles of any study design were included if the objective was to report on the introduction of anaphylaxis guidelines including diagnostic criteria and management in EDs and the pre-hospital setting. Previous systematic review articles were included if they discussed the international guidelines of anaphylactic criteria and emergency medical management. Articles were also included if they provided innovation or an improved approach to enhance the sensitivity and specificity of rapid diagnosis of anaphylaxis in emergency situations. Articles were excluded if they were not written in English, or specifically focused on prevention of anaphylaxis and allergic reaction, or pharmacological research.

Results

The electronic databases and hand search located 128 articles, however, only 18 articles met the inclusion criteria. Of these, three were literature reviews of medical treatment for anaphylaxis from the Cochrane Library. Six articles reported on the introduction of anaphylaxis guidelines and medical treatments in different countries. Three retrospective studies evaluated the efficiency of current diagnostic and management in the hospital setting. Two were international questionnaire-based surveys. There were two articles proposing diagnostic criteria and the rating method of anaphylaxis. There were two articles specifically relevant to the pre-hospital setting.

The WAO anaphylaxis guidelines have been adopted by many countries and health organisations, including the National Institute of Allergy and Infectious Diseases/Food Allergy and the Anaphylaxis Network (NIAID/FAAN) in the USA, and were

recently updated in 2011 (3,18). The guidelines include the definition, risk factors, mechanism of reaction, assessment and management of anaphylaxis (3). Table 1 shows the diagnostic criteria of anaphylaxis in the WAO guidelines.

Anaphylaxis is highly likely when any one of the following three criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg. generalised urticaria, itching or flushing, swollen lips-tongue-uvula)

And at least one of the following:

- a) Respiratory compromise (eg. dyspnoea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)
- b) Reduced blood pressure or associated symptoms of end-organ dysfunction (eg. hypotonia [collapse], syncope, incontinence)

Or

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours)

- a) Involvement of the skin-mucosal tissue (eg. generalised urticaria, itch-flush, swollen lips-tongue-uvula)
- b) Respiratory compromise (eg. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
- c) Reduced blood pressure or associated symptoms (eg. hypotonia [collapse], syncope, incontinence)
- d) Persistent gastrointestinal symptoms (eg. crampy abdominal pain, vomiting)

Or

3. Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours)
- a) Infants and children: low systolic blood pressure (age-specific) or greater than 30% decrease in systolic blood pressure
- b) Adults: systolic blood pressure of less than 90 mm Hg or greater than 30% decrease from that person's baseline

Table 1. WAO anaphylaxis criteria (3,18)

The Resuscitation Council (UK) developed emergency treatment of anaphylaxis guidelines for healthcare providers in the UK (4). The evidence-based guidelines comprised epidemiological information of anaphylaxis as well as

recognition and treatment of an anaphylactic reaction from a healthcare provider's perspective (4). The Resuscitation Council (UK) anaphylaxis guidelines provided diagnostic criteria and an algorithm for healthcare providers (4) (Table 2).

Anaphylaxis is likely when all of the following three criteria are met:

- Sudden onset and rapid progression of symptoms
- Life-threatening airway and/or breathing and/or circulation problems
- Skin and/or mucosal changes (flushing, urticaria, angioedema)

The following supports the diagnosis:

- Exposure to a known allergen for the patient

Consider:

- Skin or mucosal changes alone are not a sign of an anaphylactic reaction
- Skin and mucosal changes can be subtle or absent in up to 20% of reactions (some patients can have only a decrease in blood pressure, ie. a circulation problem)
- There can also be gastrointestinal symptoms (eg. vomiting, abdominal pain, incontinence)

Table 2. Resuscitation Council (UK) emergency treatment of anaphylactic reaction diagnostic criteria (4)

The Australian Resuscitation Council (ARC) also provided guidelines for first aid management of anaphylaxis (9). In the guidelines, they suggested a set of recognition criteria (Table 3), but give no recommendation for medical treatment (9). However, in the ARC guidelines for resuscitation in special circumstance, a peri-arrest management of anaphylaxis algorithm was provided, and was the same as the anaphylaxis algorithm in the Resuscitation Council (UK) guidelines (4,19). In addition, Ambulance Victoria Clinical Practice Guidelines (AV CPGs) provided the criteria of diagnosing anaphylaxis

including systemic involvement: angio-oedema, or urticaria, or gastrointestinal tract disturbance, and at least one of physiological distress: respiratory distress/bronchospasm, or less than adequate perfusion, or altered conscious state, observed and assessed by paramedics (20). The Australian Society of Clinical Immunology and Allergy (ASCIA) also recommended that the criteria of the severity of allergic reactions and the management by using prescribed medication, such as an EpiPen® (21) (Table 4).

Anaphylaxis encompasses a range of symptoms and signs. Diagnosis is largely based on history and physical findings. Onset can range from minutes to hours of exposure to a substance. Symptoms and signs are highly variable and may include:

- Difficult/noisy breathing
- Wheeze or persistent cough
- Swelling of face and tongue
- Swelling/tightness in throat
- Difficulty talking and/or hoarse voice
- Persistent dizziness/loss of consciousness and/or collapse
- Pale and floppy (young children)
- Abdominal pain and vomiting
- Hives, welts and body redness

Table 3. Australian Resuscitation Council anaphylaxis first aid management diagnostic criteria (9)

Ambulance Victoria clinical practice guidelines evidence of anaphylaxis (20)

Assessment for systemic involvement:

- Angio-oedema
- Urticaria
- GIT disturbance

Plus at least one of physiological distress:

- Respiratory distress/ bronchospasm
- Less than adequate perfusion
- Altered conscious state

ASCIA recommendation (21)

Mild to moderate allergic reaction:

- Swelling of lips, face, eyes
- Hives or welts
- Tingling mouth
- Abdominal pain, vomiting (these are signs of a severe allergic reaction to insects)

Severe allergic reaction (anaphylaxis)

- Difficult/ noisy breathing
- Swelling of tongue
- Swelling/ tightness in throat
- Difficulty talking and/or hoarse voice
- Wheeze or persistent cough
- Persistent dizziness or collapse
- Pale and floppy (young children)

Table 4. Anaphylactic criteria from AV CPGs and ASCIA recommendation

Brown et al and Kirkbright and Brown both provided general information about anaphylaxis (18,19). Brown et al discussed the anaphylaxis mechanism and factors that could trigger an anaphylactic reaction. In the study, they also indicated clinical features of anaphylaxis and differential diagnosis recommendations (18). However, Kirkbright and Brown provided a case study to illustrate the recognition of a real anaphylactic reaction and also highlight a few points that could increase the precision of differential diagnosis (19). These two studies did not discuss the emergency treatment of anaphylaxis.

Of the retrospective studies, Campbell et al assessed the diagnostic accuracy of the NIAID/FAAN criteria for the diagnosis of anaphylaxis in emergency department (ED) patients against those of consultant allergists (18). The results showed that NIAID/FAAN criteria are highly sensitive but less specific and are likely to be useful in the ED for the diagnosis of anaphylaxis and therefore may have some use in the pre-hospital setting (18). Similarly, Alrasbi and Sheikh examined the international guidelines for emergency management of anaphylaxis and highlighted the limitations of, and inconsistency in, the international definition of anaphylaxis and issues associated with the overall management of the anaphylaxis episode (10). Grabenhenrich et al revealed the existence of a gap between management recommendations in the guidelines and the actual management of anaphylaxis by healthcare providers (12), this issue of recommended versus actual management was also highlighted by Alrasbi and Sheikh (10). This lack of consistency in the actual management compared to the recommended management of anaphylaxis in guidelines was from studies investigating hospital based management not pre-hospital management.

Simons, on behalf of WAO, designed a survey instrument to explore the characteristics of assessment and management of anaphylaxis internationally (17). The study indicated that among all the countries that participated in the survey, four different guidelines were used, different patterns of anaphylactic reaction found, and different medications and management strategies employed in those countries (17).

Harduar-Morano et al developed an algorithm to identify potential life-threatening anaphylaxis in the ED in 2006 (22). This algorithm was based on the NIAID/FAAN anaphylaxis criteria to compare the validity of diagnosing anaphylaxis with the current International Classification of Disease, ninth revision, Clinical Modification (ICD-9-CM) diagnostic coding system (22). Brown adapted statistical methods to identify the association between clinical features of anaphylaxis and construct a grading system to differentiate the severity of reaction (23).

There were only two pre-hospital anaphylaxis studies enrolled in this review. Jacobsen and Gratton identified the challenges for paramedics and emergency physicians in diagnosing and treating patients with an anaphylactic reaction (1). Capps et al investigated the features of anaphylaxis care by ambulance

services in the UK (11). The results showed that most patients with anaphylaxis were managed without administering adrenaline in the pre-hospital setting and that first-aiders should have more training to identify the symptoms of an anaphylactic reaction and understand the use of adrenaline (11). The study also identified that both first aiders and paramedics were likely to administer adrenaline if there was respiratory or circulatory compromise, or the patient was known to have a specific allergy (11).

Discussion

This study was carried out to identify appropriate diagnostic criteria and emergency treatment of anaphylaxis for use in the pre-hospital setting. By reviewing current anaphylaxis criteria and medical treatment it is evident that there is no universal agreement on the diagnosis and treatment of anaphylaxis (3,4,9,19,24,25). Even in the pre-hospital setting there are few studies reporting specific criteria for paramedics to develop an explicit criteria and treatment for anaphylaxis internationally (1,11).

The WAO guidelines, Resuscitation Council (UK) guidelines and the ARC guidelines show different methods for defining and diagnosing an anaphylactic reaction (3,4,19). The similarity between the WAO guidelines and those from the Resuscitation Council (UK) is that they both indicate three major clinical features of anaphylaxis: rapid onset of an illness, life-threatening vital signs and skin and/or mucosal changes (3,4). On the other hand, the ARC guidelines are similar to the UK Resuscitation Council's in that they adopted the UK Resuscitation Council's guidelines of anaphylaxis algorithm in relation to resuscitation in special circumstance, however, they do not do so in the section that refers to anaphylaxis specifically. The ASCIA would appear to have the defined the allergic reaction and anaphylaxis better than the resuscitation councils and advocate the early administration of adrenaline (21). The resuscitation councils and Ambulance Victoria advocate the use of adrenaline at a later, more severe stage of the allergic reaction/anaphylaxis episode (20). In all guidelines adrenaline is the primary drug of choice in the management of anaphylaxis.

There have been no pre-hospital specific studies that have investigated the best dose of adrenaline for managing anaphylaxis. An issue that requires further investigation is the dose of adrenaline for the management of anaphylaxis. The dose internationally varies between 0.3 mg (17) to 0.5 mg (4) for adults with the child dose showing similar variation. From a paramedic's perspective it is difficult to rapidly identify a patient with anaphylaxis by using the criteria in the above guidelines. Instead, paramedics have to assess and treat life-threatening conditions successively starting from airway, breathing and circulation in order to ensure a patient's fatal risk during anaphylaxis is reduced. The UK Resuscitation Council guidelines provide a similar pathway to the initial patient assessment in paramedic practice.

However, the signs and symptoms of anaphylaxis may not appear the same as listed in guidelines. The criteria outlined by the ASCIA are more simplistic and appear easier to follow for lay people and healthcare providers, including the early administration of adrenaline. Either way, healthcare providers should be provided with the range of clinical features for allergic reaction and anaphylaxis and encouraged to administer adrenaline earlier if they are in doubt about the severity of the allergic episode (1,10). The criteria outlined by the ASCIA better cover the hyperactive immune response to an antigen, which may present as an anaphylactic reaction, as it is more broad in its definition of an allergic reaction (21).

Adrenaline is seen as the first line treatment for anaphylaxis, but there is a lack of high quality scientific evidence to support its use in the pre-hospital setting (11). Antihistamines and glucocorticoids may also be used in the treatment of anaphylaxis, with minimal level one evidence to support their use (1,14,15). The challenge would be the ethical issue of addressing a randomised trial in a group of patients with life-threatening conditions when adrenaline is known to reverse the clinical manifestations of anaphylaxis.

The diagnosis of anaphylaxis might influence the treatment in patients. Due to a wide range of signs and symptoms derived from an anaphylactic reaction, a definition of anaphylaxis severity might assist healthcare providers to determine the treatment plan for patients (23). The treatment might be based on the rapid management of life-threatening signs and symptoms managed with adrenaline while severe reactions might be treated by other slow onset medication, such as antihistamine, in the pre-hospital setting. The criteria for severe allergic reaction by the ASCIA is broader than other definitions but it appears to be more representative of the disease as

anaphylaxis can present in varying ways according to the allergen and the person's response to that allergen, injected or absorbed.

Limitations of this study

The findings of this study are potentially limited as there is a lack of anaphylaxis studies specific to the pre-hospital setting. The use of ED study results might not completely fit the pre-hospital environment. There is also the potential that articles published in languages other than English and journals not listed in the electronic databases may have been missed.

Conclusion

Anaphylaxis is a potentially life-threatening medical emergency and a challenge for emergency healthcare providers. The inconsistency of definition and diagnosis criteria increases the risk of under-diagnosis and under-treatment in patients with anaphylaxis. The presenting clinical features may vary depending on the aetiology, immune response and target organ. Emergency healthcare providers need a more explicit set of diagnosis criteria and treatment regimens to rapidly relieve a patient's anaphylactic reaction and potentially life-threatening situation.

Competing interests

The authors declare they have no competing interests.

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