

Editorial

Evidence-based management of anaphylaxis

F. E. R. Simons¹, A. Sheikh²

¹Department of Pediatrics & Child Health, Department of Immunology, Canadian Institutes of Health Research National Training Program in Allergy & Asthma, Faculty of Medicine, University of Manitoba, Manitoba, Canada; ²Allergy & Respiratory Research Group, Division of Community Health Sciences: GP Section, University of Edinburgh, Edinburgh, UK

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Dr F. E. R. Simons
820 Sherbrook Street
Winnipeg Manitoba
Canada R3A 1R9

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For common diseases such as asthma and allergic rhinitis, many efficacious and safe interventions, both pharmacological and nonpharmacological, have been introduced in recent decades. Thousands of prospective, randomized, masked, controlled clinical trials of these interventions have been conducted in large numbers of patients with well-defined symptoms and symptom patterns, and with different levels of disease severity. Newer interventions have been compared with placebo and, increasingly, with more established treatments. The information obtained from these studies has been systematically identified, collated, critically appraised for its validity and usefulness, and summarized (with attention paid to the issue of potential bias) in Cochrane Collaboration reviews and other systematic reviews. Based on relatively abundant evidence, consistent, high-quality recommendations for management of asthma and allergic rhinitis have been promulgated in national and international guidelines (1–3). Most doctors now accept the concept that evidence-based interventions in these diseases are superior to tradition- and opinion-based interventions (4).

In contrast, the state of the evidence base for the treatment of anaphylaxis has not yet been as thoroughly examined, although recent attempts have been made in this regard (5–7). There are no universally accepted guidelines for pharmacological or nonpharmacological interventions in anaphylaxis; indeed, the definition of the disease continues to evolve (8–11). Anaphylaxis is still

considered to be uncommon (12), although the rate of occurrence is increasing (13). Many of the pharmacologic agents available for use in anaphylaxis, for example, adrenaline, first-generation H₁-antihistamines such as diphenhydramine, and glucocorticoids, are more than half a century old, and were therefore introduced long before the era of evidence-based medicine.

Moreover, when the principles of evidence-based medicine are applied to interventions in anaphylaxis, other concerns become apparent. For a number of reasons, it is difficult to conduct prospective, randomized, double-masked, placebo-controlled trials in this disease. Most cases of anaphylaxis now occur unpredictably in community settings although they also still occur in healthcare settings despite vigilant preventive efforts. The clinical presentation of anaphylaxis is characterized by variability among patients, and variability in the same patient from one episode to another. For example, the time lag between exposure to the trigger and the onset of symptoms can vary from minutes to hours. The severity of symptoms can vary from mild and self-limited to fatal within minutes. The number of symptoms can vary from a few to many symptoms in virtually all body systems (11, 14).

For over a decade, the Cochrane Collaboration has led the way in setting high standards for systematic reviews of the evidence base for diagnostic and therapeutic procedures. This approach is widely accepted as the gold standard, and has helped to identify the quality of the

scientific evidence on which treatment is based, including grey zones where the evidence is incomplete or conflicting. Several years ago, when we embarked on a journey to assess the quality of current evidence for management of anaphylaxis, and approached the Cochrane Collaboration for registration of protocols, it became apparent that the best home in the Collaboration for our proposed protocols was, in fact, with the Anaesthesia Group. This was of considerable interest because historically, anaesthesiologists were among the earliest groups of specialist doctors to investigate the recognition and management of anaphylaxis (15). Currently, however, as noted previously, many individuals with anaphylaxis experience the episode in their home or in some other community setting, far from the expert assistance of any doctor, let alone an anaesthesiologist!

A summary of the first of our several Cochrane Collaboration reviews on interventions in anaphylaxis is included in this issue of *Allergy* (16). We began with H₁-antihistamines because they are the most commonly used treatment for anaphylaxis (17, 18). A critical appraisal of the evidence base for treatment with adrenaline in anaphylaxis will be published shortly (19), and

this will be followed by a Cochrane Collaboration review investigating the role of glucocorticoids in anaphylaxis treatment. In all these reviews, we seek to focus on the highest order evidence, namely, that derived from randomized, controlled trials, but in the absence of such trials, to make reference to findings from other investigations with less reliable study designs. By drawing attention to the state of the evidence base for the treatment of anaphylaxis, we hope to provide a unique perspective on the treatment of this disease, to help doctors become more confident in addressing some of the quandaries they face in making clinical decisions for anaphylaxis management (20), and to stimulate research in this critically important area.

We gratefully acknowledge the support of the Cochrane Collaboration, our co-authors and our reviewers who, in the Cochrane Collaboration tradition, include members of the general public. Finally, we thank our esteemed colleague, Professor Jean Bousquet, a well-known champion of evidence-based medicine (1, 3, 4), for making the results of these Cochrane collaboration reviews accessible in *Allergy* and thereby bringing them to the attention of the allergy/immunology community worldwide.

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