

Commentary

Commentary on ‘Glucocorticoids for the treatment of anaphylaxis’

This is a commentary on a Cochrane review, published in the issue of EBCH, first published as: Choo KJL, Simons FER, Sheikh A. Glucocorticoids for the treatment of anaphylaxis. *Cochrane Database of Systematic Reviews* 2012, Issue 4. Art. No.: CD007596. DOI: 10.1002/14651858.CD007596.pub3.

Evidence-Based Child Health: a Cochrane Review Journal is now indexed by MEDLINE (<http://www.ncbi.nlm.nih.gov/pubmed>) and Scopus (<http://www.scopus.com>)

Commentary by Alexandra F. Santos and Gideon Lack

The administration of systemic glucocorticosteroids to patients with anaphylaxis is common (1) and is increasing (2) in parallel with the increase in the incidence of anaphylaxis, which is particularly evident in the paediatric age groups. Although a short course of glucocorticosteroids is usually safe, is it actually effective?

The Cochrane review by Choo *et al.* (3) found no randomized- or quasi-randomized-controlled studies assessing the effectiveness of glucocorticosteroids in the treatment of anaphylaxis. In recent anaphylaxis guidelines (4), glucocorticosteroids appear as a third-line therapy to reduce the risk of late-phase respiratory symptoms. The rationale behind the use of glucocorticosteroids in anaphylaxis is an extrapolation from their effectiveness in acute exacerbations of asthma, where they have shown to reduce the need for admission to hospital and to prevent relapses (5, 6). Glucocorticosteroids are also thought to be able to prevent the development of biphasic and protracted anaphylaxis symptoms. Protracted and biphasic anaphylaxis occur in a minority of cases (<1–20%) and have been defined as anaphylaxis symptoms that persist (protracted) or recur (biphasic) up to 72 hours after the initial symptoms without additional exposure to the trigger. But what is the underlying mechanism? Is this due to massive immediate mediator release that overcomes the ability of pharmacologic treatment to control their effects, or is it due to the late-phase allergic inflammation, or to a second immediate-type response secondary to the trigger that persists in circulation (e.g. due to continued absorption of food allergens)? The mechanism of protracted anaphylaxis may be different from that of biphasic reactions. The predicted effectiveness of systemic glucocorticosteroids in biphasic or prolonged anaphylactic reactions would depend on the answer to these questions.

Systemic glucocorticosteroids exert their potent anti-inflammatory action by modifying gene expression; thus their effects are not seen until a few hours following administration. Glucocorticosteroids have shown to be able to inhibit the late phase of the inflammatory response following allergen challenge, but not the immediate phase (7, 8). Therefore, one would expect systemic corticosteroids to reduce anaphylaxis symptoms that are due to the late-phase inflammatory response, i.e. the second round of mediator release and infiltration of inflammatory cells; however, they may not have any effect on a protracted reaction that is due to overwhelming immediate mediator release or on a biphasic reaction that is due to a repeated immediate-type response to the trigger.

To clarify the effectiveness of glucocorticosteroids in the treatment of anaphylaxis, a randomized, double-blind controlled trial of systemic glucocorticosteroid versus placebo in patients with anaphylaxis is needed. The outcomes of this trial would be the incidence of symptoms of anaphylaxis up to 72 hours after the initial episode. In addition, biological samples should be collected during this period to help understanding the underlying mechanism of the observed clinical response to the treatment.

While further research is awaited, it is important to bear in mind that glucocorticosteroids have no effect in the immediate inflammatory response and thus should not be given in place or delay the administration of adrenaline and other first- and second-line emergency treatments. Glucocorticosteroids may be empirically given in the context of anaphylaxis to prevent late-phase respiratory symptoms, but its effectiveness in the treatment of acute, protracted and biphasic anaphylaxis has not yet been proven.

Declaration of interest

No conflicts of interest.

Alexandra F. Santos^{1,2,3*} and Gideon Lack¹

¹Department of Pediatric Allergy, Division of Asthma, Allergy & Lung Biology, King's College London-MRC & Asthma UK Centre in Allergic Mechanisms of Asthma, London, UK

²Immunology Department, Coimbra University Hospital, Coimbra, Portugal

³Gulbenkian Programme for Advanced Medical Education, Lisbon, Portugal

*Correspondence to: Alexandra F. Santos, MD, MSc, Department of Pediatric Allergy, Division of Asthma, Allergy and Lung Biology, King's College London, 5th floor Tower Wing, Guy's Hospital, London SE1 9RT, UK.

E-mail: alexandra.santos@kcl.ac.uk

Keywords: anaphylaxis, biphasic, corticosteroids, glucocorticoids, glucocorticosteroids, late-phase

References

1. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF Jr, 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. *Ann Emerg Med* 2006; **47**: 373–380.
2. Gaeta TJ, Clark S, Pelletier AJ, Camargo CA. National study of US emergency department visits for acute allergic reactions, 1993 to 2004. *Ann Allergy Asthma Immunol* 2007; **98**: 360–365.
3. Choo KJ, Simons FE, Sheikh A. Glucocorticoids for the treatment of anaphylaxis. *Cochrane Database Syst Rev* 2012; **4**: CD007596.
4. Roberts G, Muraro A, Worm M, Bilò MB, Brockow K, Fernández-Rivas M, *et al.* Anaphylaxis: guideline from the European Academy of Allergology and Clinical Immunology. *Allergy* 2013 (in preparation).
5. Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev* 2001; **1**: CD002178.
6. Rowe BH, Spooner CH, Ducharme FM, Bretzlaff JA, Bota GW. Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database Syst Rev* 2007; **3**: CD000195.
7. Liu MC, Proud D, Lichtenstein LM, Hubbard WC, Bochner BS, Stealey BA, *et al.* Effects of prednisone on the cellular responses and release of cytokines and mediators after segmental allergen challenge of asthmatic subjects. *J Allergy Clin Immunol* 2001; **108**: 29–38.
8. Pipkorn U, Proud D, Lichtenstein LM, *et al.* Effect of short-term systemic glucocorticoid treatment on human nasal mediator release after antigen challenge. *J Clin Invest* 1987; **80**: 957–961.

If you would like to make a comment on the above article, you are invited to submit a letter to the Editor by email (child@ualberta.ca). Selected letters may be edited and published in future issues of the journal.