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[Intervention Review]

Glucocorticoids for the treatment of anaphylaxis

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ABSTRACT

Background

Anaphylaxis is a serious hypersensitivity reaction that is rapid in onset and may result in death. Anaphylaxis guidelines recommend glucocorticoids for the treatment of people experiencing anaphylaxis.

Objectives

We sought to assess the benefits and harms of glucocorticoid treatment during episodes of anaphylaxis.

Search methods

In our previous version we searched the literature until September 2009. In this version we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 3), MEDLINE (Ovid) (1956 to September 2011), EMBASE (Ovid) (1982 to September 2011), CINAHL (EBSCOhost) (to September 2011). We also searched the UK National Research Register and websites listing ongoing trials, and contacted international experts in anaphylaxis in an attempt to locate unpublished material.

Selection criteria

We planned to include randomized and quasi-randomized controlled trials comparing glucocorticoids with any control (either placebo, adrenaline (epinephrine), an antihistamine, or any combination of these).

Data collection and analysis

Two authors independently assessed articles for inclusion.

Main results

We found no studies that satisfied the inclusion criteria.

Authors' conclusions

We are, based on this review, unable to make any recommendations for the use of glucocorticoids in the treatment of anaphylaxis.

PLAIN LANGUAGE SUMMARY

Glucocorticoids for the treatment of anaphylaxis

Glucocorticoids for the treatment of anaphylaxis (Review)

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Anaphylaxis is a serious allergic reaction that is rapid in onset and may result in death. It is commonly triggered by a food, insect sting, medication, or natural rubber latex. The reaction typically occurs without warning and can be a frightening experience both for those at risk and their families and friends. Steroids (glucocorticoids) are often recommended for use in the management of people experiencing anaphylaxis. However, the evidence base in support of the use of steroids is unclear. We therefore conducted a systematic review of the literature, searching key databases for high quality published and unpublished material on the use of steroids for the emergency treatment of anaphylaxis. In addition, we contacted experts in this health area and the relevant pharmaceutical companies. We were unable to find any randomized controlled trials on this subject through our searches. We conclude that there is no evidence from high quality studies for the use of steroids in the emergency management of anaphylaxis. Therefore, we can neither support nor refute the use of these drugs for this purpose.

BACKGROUND

Description of the condition

Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death (Sampson 2006). There is some evidence that the incidence of anaphylaxis is increasing (Decker 2008; Gupta 2003; Gupta 2007; Lin 2008; Poulos 2007; Sheikh 2001; Sheikh 2008). The lifetime risk may be as high as one in 100 individuals in the general population (Lieberman 2006; Neugut 2001; Simons 2002). There are many possible triggers, including food, insect venoms, medication and biologics, anaesthetics, diagnostic agents, natural rubber latex, vaccinations for prevention of infectious diseases, and exercise (Brown 2001; Brown 2004; Kemp 2002; Peng 2004; Sampson 2005; Simons 2006; Simons 2009). In some individuals anaphylaxis is idiopathic (Webb 2006). During an episode of anaphylaxis, some 80% to 90% of individuals experience flushing, itching, hives, angioedema, or other skin or mucosal symptoms; up to 70% have stridor, dysphonia, cough, chest tightness, shortness of breath, wheezing, or other respiratory symptoms; and up to 45% have vomiting, diarrhoea, or cramp-like abdominal pain. Of note only 10% to 45% have cardiovascular symptoms, including chest pain, hypotension, or shock (Brown 2001; Brown 2004; Sampson 2006). Signs and symptoms usually occur within five to 30 minutes of exposure to the trigger, although occasionally they may not develop for hours, yet anaphylaxis may be fatal within minutes (Bock 2001; Bock 2007; Greenberger 2007; Pumphrey 2000; Pumphrey 2003; Pumphrey 2007; Sampson 1992). The signs, symptoms, and treatment of anaphylaxis are similar regardless of the trigger or the pathogenesis (Simons 2008).

Biphasic (late-phase) and protracted reactions occur in from < 1% to 20% of people with anaphylaxis. Most of these reactions are mild or moderate (Confino-Cohen 2010; Scranton 2009; Smit 2005). Fatalities appear to be rare. Risk factors for biphasic reactions include a severe initial reaction, presence of laryngeal oedema or hypotension, delay in the administration of adrenaline (epinephrine), too small a dose of adrenaline, and a history of a previous biphasic reaction (Douglas 1994; Ellis 2007; Lieberman 2005; Stark 1986).

Description of the intervention

Although adrenaline remains the main treatment for people experiencing anaphylaxis, glucocorticoids are given after the initial resuscitation period (Badger 2004; Chin 2004; Joint Task Force 2005; Korenblat 1999; Orbach 2005; Sampson 2006; Walters 2005). Indeed, in recent retrospective multi-centre studies in emergency departments glucocorticoids were reported to be more frequently administered than adrenaline, traditionally the initial treatment of choice in anaphylaxis (Clark 2004; Clark 2005; Gaeta 2007; McLean-Tooke 2003; Simons 2004a; Simons 2004b). This is in agreement with reports that glucocorticoid use for anaphylaxis is increasing (Gaeta 2007). H₁-antihistamines are also commonly administered in anaphylaxis, despite the lack of published evidence for this intervention (Sheikh 2007; Simons 2004c).

Current Resuscitation Council (UK) Guidelines for the Treatment of Anaphylaxis (Anaphylaxis UK Guidelines) recommend giving hydrocortisone 200 mg by intramuscular or slow intravenous injection after the initial resuscitation, for the treatment of adults or children more than 10 years of age. Other guidelines recommend methylprednisolone, triamcinolone, or prednisone by intravenous,

intramuscular, or oral routes using different doses and dose regimens (Brown 2006; Joint Task Force 2005; Kemp 2002; Muraro 2007; Sampson 2005; Sampson 2006; Soar 2008). Glucocorticoid administration in anaphylaxis usually consists of either a single dose or a dose on the day of the event followed by a dose on each of the next few days.

How the intervention might work

The primary action of glucocorticoids is down-regulation of the late-phase eosinophilic inflammatory response, as opposed to the early-phase response. Short-term glucocorticoid treatment is seldom associated with adverse effects (Schleimer 2008).

Why it is important to do this review

There are uncertainties as to whether glucocorticoids administered for the treatment of anaphylaxis can prevent or ameliorate biphasic or protracted reactions. There is published evidence that they might be ineffective in this regard (Douglas 1994; Ellis 2007; Lieberman 2005; Stark 1986). The existing evidence for the use of glucocorticoids appears to consist mainly of retrospective studies, case reports, and other descriptive literature. A more comprehensive and structured search for literature on the benefits and risks of short-term glucocorticoid treatment in anaphylaxis is required in order to ascertain if, indeed, there is reasonable evidence for continuing to recommend glucocorticoid use in the treatment of this potentially life-threatening disease.

OBJECTIVES

We sought to assess the benefits and harms of glucocorticoid treatment during episodes of anaphylaxis. We defined anaphylaxis as any serious systemic allergic reaction that is rapid in onset with potentially fatal manifestations. Such reactions usually involve more than one body system (for example skin, respiratory, gastrointestinal, or cardiovascular). We sought to include all anaphylactic events regardless of mechanism or trigger.

METHODS

Criteria for considering studies for this review

Types of studies

We did not distinguish between anaphylactic and anaphylactoid (also sometimes termed pseudoallergic) reactions in this review. We looked for randomized controlled trials (RCTs) comparing glucocorticoids with any control treatment (either placebo, adrenaline (epinephrine), antihistamine, or any combination of these).

Because we anticipated identifying very few, if any, RCTs investigating the treatment of anaphylaxis, we were also interested in quasi-randomized trials where the method of allocation was not truly random (for example consecutive allocation to each treatment group). We planned to apply the Cochrane approach using the methods detailed in Section 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to assess the quality of both randomized and quasi-randomized studies.

Types of participants

We were interested in including all patients (infants, children, and adults; in hospital or other healthcare facility) experiencing an

anaphylactic reaction caused by food, insect venoms, medication and biologics, anaesthetics, diagnostic agents, vaccinations for infectious disease, natural rubber latex, exercise, or any other trigger, as well as idiopathic disease.

Types of interventions

We were interested in any intervention with any glucocorticoid administered through any route (intravenous, intramuscular, or oral) in any dose or dose regimen. We excluded studies focusing on the use of glucocorticoids for the prevention of anaphylaxis.

Types of outcome measures

Our outcome measures of interest were as follows.

Primary outcomes

1. Mortality rate

Secondary outcomes

2. Prevention of biphasic or prolonged anaphylaxis (symptoms persisting or recurring in from one to 72 hours without any ongoing or additional exposure to the trigger) (Lieberman 2005; Sampson 2006)
3. Incidence of cardiovascular manifestations, e.g. chest pain, palpitations, shock
4. Incidence of respiratory manifestations, e.g. shortness of breath, cough, wheeze or stridor
5. Incidence of gastrointestinal manifestations, e.g. abdominal pain, diarrhoea, nausea, vomiting
6. Incidence of other clinical manifestations as included in the studies, e.g. neurological manifestation such as loss of consciousness or headaches, or skin manifestations such as urticaria, erythema, or oedema

Health service use

7. Hospitalization rate
8. Length of emergency department visit*
9. Length of hospital stay*
10. Rate of re-presentation to hospital
11. Incidence of any adverse events reported for any treatment delivered

*We acknowledged that the lengths of stay outcomes may be difficult to interpret given that worse clinical outcomes may be associated with shorter hospital stays. In the event of finding such data, we planned to interpret the outcomes with care and in the context of clinical outcomes.

Search methods for identification of studies

Electronic searches

In our previous version we searched the literature until September 2009. In this version we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 3)

using the following key words: anaphylaxis and glucocorticoids (see [Appendix 1](#)).

We searched MEDLINE (Ovid) (1956 to September 2011), see [Appendix 2](#); EMBASE (Ovid) (1982 to September 2011), see [Appendix 3](#); and CINAHL (EBSCOhost) (1982 to September 2011), see [Appendix 4](#) using the Cochrane RCT filter (Higgins 2011).

We did not apply any language restriction.

Searching other resources

In an attempt to uncover additional relevant published data, grey literature, unpublished data, and research in progress, we also:

- developed a database of first and last authors of potentially eligible studies and searched the Science Citation Index Expanded (SCI-EXPANDED) (1945 to 2009) using these names;
- searched the bibliographies of identified studies;
- compiled a database of international experts in anaphylaxis;
- contacted relevant pharmaceutical companies;
- searched the UK National Research Register;
- searched websites listing ongoing trials, such as <http://clinicaltrials.gov/>, <http://www.controlledtrials.com/>, and <http://www.actr.org.au/>.

Data collection and analysis

Three authors (AS, KC, and ES) undertook this review; KC co-ordinated the review.

Selection of studies

Two authors (KC and AS) ran the searches as detailed in the search strategy. Both authors independently reviewed titles and abstracts from the literature searches to identify relevant trials for full review. We planned to retrieve the full text copies of all potentially eligible studies and subject each to independent review using the inclusion criteria detailed above. KC wrote to authors of papers for additional information and screened responses for relevance as per the inclusion criteria.

We planned to resolve any disagreements by discussion between authors. In the case of consensus not being reached, we planned to involve the third author (ES) both to participate and, if necessary, arbitrate in the final decision.

Data extraction and management

Two authors (KC and AS) planned to independently extract data using a suitably adapted version of the data extraction form developed by the Cochrane Anaesthesia Review Group. We planned to resolve any disagreements by discussion between the authors; in the case of consensus not being reached, we planned to involve the third author (ES) both to participate and, if necessary, arbitrate in the final decision.

Assessment of risk of bias in included studies

In our previous version we planned to grade each parameter of trial quality as: A, low risk of bias; B, moderate risk of bias; C, high risk of bias. We planned to make an overall assessment for each randomized controlled trial using the same rating scale.

In this updated version of the review we planned to assess the quality of included RCTs following the Cochrane approach using the methods detailed in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We planned to concentrate on using the following five parameters to assess quality:

- random sequence generation;
- allocation concealment;
- blinding of participants, personnel, and outcome assessors;
- incomplete outcome data;
- selective reporting;
- other bias.

We planned to judge each parameter of trial quality as either: low risk of bias; high risk of bias; or unclear; and make an overall assessment for each RCT using the same grading system.

We planned to document the methodological quality of these trials (both randomized and quasi-randomized) following the Cochrane approach, using the methods detailed in Section 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Two authors (KC and AS) planned to independently assess study quality; we did not plan to mask review authors to study details. We planned to assess the agreement of authors on methodological quality assessment and to resolve disagreements by discussion and, if necessary, with the involvement of a third author (ES).

Measures of treatment effect

We intended to provide a risk ratio (RR) or mean difference for the primary outcome of each trial included, on the basis of an intention-to-treat analysis.

Unit of analysis issues

We anticipated that included studies would most likely follow a parallel group design, with individuals randomized to one of two arms of the trial. We did not anticipate identifying any cluster-randomised trials in this review.

Dealing with missing data

In any studies with missing data, in line with recommendations in the Cochrane Handbook, Section 16.1.2 (Higgins 2011), we intended to contact the authors for further information. In the event of being unable to obtain such information we would have reported this and discussed its potential impact. We did not intend to impute the missing data.

Assessment of heterogeneity

We planned to test for heterogeneity using the I^2 statistic and significant heterogeneity would have been assumed if I^2 was greater than 40% (that is more than 40% of the variability in outcome between trials could not be explained by sampling variation) (Higgins 2011).

Assessment of reporting biases

We planned to assess for selective reporting of outcomes by, where possible, comparing outcome measures listed in trial protocols and the published reports. Furthermore, we planned to assess for evidence of publication bias graphically using funnel plots and statistically using the Begg and Egger tests (Begg 1994; Egger 1997).

Data synthesis

We proposed to use Review Manager (RevMan 5.1) for data analysis and quantitative data synthesis. For dichotomous data, we planned to calculate individual and pooled statistics as relative risks (RR) with 95% confidence intervals (CI). For continuous data, we planned to calculate individual and pooled statistics as mean differences (MD) or standardized means differences with 95% CI. We planned to give consideration to the appropriateness of meta-analysis in the presence of significant clinical or statistical heterogeneity. We planned to undertake meta-analysis using fixed-effect or random-effects modelling, depending on whether or not data were found to be homogenous. In the absence of any statistically significant between study heterogeneity, we planned to report a pooled effect derived from the fixed-effect model. If we uncovered statistical heterogeneity, however, we planned to investigate this (see subgroup analysis and investigation of heterogeneity section). In the event of such a scenario, and if still considered clinically appropriate to pool data, we will report a pooled effect derived from the random-effects model in future updates. We planned to undertake quantitative analyses of outcomes, wherever possible, on an intention-to-treat basis.

Subgroup analysis and investigation of heterogeneity

We were interested in analysing data for the following subgroups.

1. Mild versus moderate versus severe anaphylaxis (Brown 2004).
 - Mild reactions (involving the skin and mucosa only): generalized erythema, urticaria, or angioedema including periorbital oedema.
 - Moderate reactions (features suggesting gastrointestinal, cardiovascular, or respiratory involvement): dyspnoea, stridor, wheeze, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness, or abdominal pain.
 - Severe reactions (hypoxia, hypotension, or neurological compromise): cyanosis or saturation of peripheral oxygen (SpO_2) < 92% at any stage, hypotension (systolic blood pressure < 90 mm Hg in adults, confusion, collapse, loss of consciousness, or incontinence).
2. Mode of administration of treatment (e.g. intravenous versus intramuscular versus oral).
3. Time from onset of first anaphylaxis symptoms to receiving treatment.
4. Age (infants, children, adolescents, adults, and the elderly).
5. Different glucocorticoids according to the agent(s) used in each study.

Sensitivity analysis

We planned to undertake sensitivity analysis for the allocation of missing data by best and worst case analysis and also sensitivity analysis on the basis of only including randomized studies. This would have allowed an assessment of the impact on the review conclusions of excluding studies judged to be at high risk of bias.

RESULTS

Description of studies

There were no eligible studies (see table 'Characteristics of included studies').

Results of the search

We searched the databases up to September 2011. Our search revealed 1764 hits (see [Figure 1](#)). We screened 1587 records after we removed duplicates. After scrutiny of the remaining 18 abstracts, we did not find any studies that fulfilled the inclusion criteria. We searched websites listing ongoing trials, using anaphylaxis as a keyword, but failed to identify any potential studies. We contacted experts in the field of anaphylaxis but this also failed to contribute any relevant studies, published or unpublished.

Figure 1. Study flowchart (PRISMA template)

Included studies

There were no eligible studies (see table 'Characteristics of included studies').

Excluded studies

There were no eligible studies (see table 'Characteristics of excluded studies').

Risk of bias in included studies

There were no eligible studies.

Allocation

There were no eligible studies.

Blinding

There were no eligible studies.

Incomplete outcome data

There were no eligible studies.

Selective reporting

There were no eligible studies.

Other potential sources of bias

There were no eligible studies.

Effects of interventions

There were no eligible studies.

DISCUSSION

Summary of main results

This comprehensive review failed to identify any relevant randomized or quasi-randomized controlled trial evidence for the effectiveness of glucocorticoids in the management of people experiencing anaphylaxis. This contrasts with the important role of glucocorticoids in the prevention and treatment of asthma and other allergic disorders. In view of the difficulties of conducting research in an emergency context, this is not a particularly surprising finding ([Simons 2007](#); [Simons 2008](#)). Clinicians should nonetheless be aware of the lack of a strong evidence base for the use of a glucocorticoid for the treatment of anaphylaxis. A clear statement should be made to this effect in anaphylaxis guidelines ([Alrasbi 2007](#)). Although there is little direct evidence of harm associated with use of glucocorticoids, there is, as noted above, persistent evidence that glucocorticoids are often inappropriately used as the first-line agent in place of adrenaline, which is more likely to prove life-saving ([Sheikh 2008b](#); [Soar 2008](#)). Consideration, therefore, needs to be given to conducting a randomized controlled trial ([Simons 2008](#)).

Overall completeness and applicability of evidence

We found no relevant evidence.

Quality of the evidence

We found no relevant evidence.

Potential biases in the review process

There is always the possibility that our searches failed to identify all relevant studies; we feel that this is, however, unlikely in the context of this review.

Agreements and disagreements with other studies or reviews

We are not aware of any other systematic reviews on this subject.

AUTHORS' CONCLUSIONS

Implications for practice

We found no relevant evidence for the use of glucocorticoids in the treatment of an acute episode of anaphylaxis. We are, therefore, unable to make any new recommendations based on the findings of this review. While we do not necessarily suggest that anaphylaxis guidelines no longer recommend glucocorticoids, these guidelines need to be more explicit about the basis of their recommendations regarding the use of these agents ([Alrasbi 2007](#)).

Implications for research

There is a need for a more robust evidence base for the use of glucocorticoids in the treatment of anaphylaxis. Conducting trials in the context of a potentially life-threatening emergency is fraught with difficulties but, considering that glucocorticoids are not recommended as a first-line agent in anaphylaxis guidelines, it may be feasible to conduct experimental studies. Any future trials would need to consider in particular:

- appropriate sample size with power to detect expected difference;
- careful definition and selection of target patients;
- appropriate comparator therapy;
- appropriate outcome measures;
- careful elucidation of any adverse effects;
- the cost-effectiveness of the therapy;
- appropriate safety measures, i.e. treatment with adrenaline injection(s), supplemental high-flow oxygen, and intravenous fluid resuscitation;
- placement in the recumbent position or position of comfort with elevation of lower extremities;
- appropriate continuous non-invasive monitoring of heart rate, blood pressure, and oxygenation; and
- appropriately equipped healthcare facility with professionals who are trained and experienced with diagnosing and treating anaphylaxis.

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APPENDICES

Appendix 1. Search strategy for CENTRAL and The Cochrane Library

#1 MeSH descriptor Anaphylaxis explode all trees
#2 anaph?l* or (acute near allerg*)
#3 (#1 OR #2)
#4 MeSH descriptor Hydrocortisone explode all trees
#5 MeSH descriptor Prednisolone explode all trees
#6 MeSH descriptor Betamethasone explode all trees
#7 MeSH descriptor Clobetasol explode all trees
#8 MeSH descriptor Cortisone explode all trees
#9 MeSH descriptor Anti-Inflammatory Agents explode all trees
#10 MeSH descriptor Immunosuppressive Agents explode all trees
#11 MeSH descriptor Pregnenediones explode all trees
#12 MeSH descriptor Glucocorticoids explode all trees
#13 MeSH descriptor Triamcinolone Acetonide explode all trees
#14 MeSH descriptor Triamcinolone explode all trees
#15 MeSH descriptor Drug Hypersensitivity explode all trees
#16 prednisolone or betamethasone or cortison* or deflazacort or calcort or dexamethasone or hydrocortisone or efcortisol or hydrocortone or solu-cortef or methylprednisolone or solu-medrone or depo-medrone or triamcinolone or kenalog
#17 (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)
#18 (#3 AND #17)

Appendix 2. Search Strategy for MEDLINE (OvidSP)

#1. exp Anaphylaxis/
#2. (anaph?l* or (acute adj3 allerg*)).mp.
#3. #1 or #2
#4. exp Hydrocortisone/ or exp Prednisolone/ or exp Betamethasone 17-Valerate/ or exp Betamethasone/ or exp Clobetasol/ or exp Cortisone/ or exp Anti-Inflammatory Agents/ or exp Immunosuppressive Agents/ or exp Pregnenediones/ or exp Glucocorticoids/ or exp Prednisone/ or exp Dexamethasone Isonicotinate/ or exp Dexamethasone/ or exp Steroids/ or exp Methylprednisolone/ or exp Triamcinolone Acetonide/ or exp Triamcinolone/ or exp Drug Hypersensitivity/
#5. (prednisolone or betamethasone or cortison* or deflazacort or calcort or dexamethasone or hydrocortisone or efcortisol or hydrocortone or solu-cortef or methylprednisolone or solu-medrone or depo-medrone or triamcinolone or kenalog).mp.
#6. #4 or #5
#7. #3 and #6
#8. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (animals not (humans and animals)).sh.
#9. #7 and #8

Appendix 3. Search strategy for EMBASE (OvidSP)

#1. exp anaphylaxis/
#2. (anaph?l* or (acute adj3 allerg*)).mp.
#3. #1 or #2
#4. hydrocortisone/ or prednisolone/ or betamethasone valerate/ or betamethasone/ or clobetasol/ or cortisone/ or antiinflammatory agent/ or pregnane derivative/ or glucocorticoid/ or prednisone/ or dexamethasone isonicotinate/ or dexamethasone/ or steroid/ or methylprednisolone/ or triamcinolone acetonide/ or triamcinolone/ or drug hypersensitivity/
#5. (prednisolone or betamethasone or cortison* or deflazacort or calcort or dexamethasone or hydrocortisone or efcortisol or hydrocortone or solu-cortef or methylprednisolone or solu-medrone or depo-medrone or triamcinolone or kenalog).ti,ab.
#6. #4 or #5
#7. #3 and #6
#8. (placebo.sh. or controlled study.ab. or random*.ti,ab. or trial*.ti,ab.) not (animals not (humans and animals)).sh.
#9. #7 and #8

Appendix 4. Search strategy for CINAHL (EBSCOhost)

S1 (MM "Anaphylaxis")
S2 TX anaphyl* or (acute allerg*)
S3 S1 or S2
S4 TX (prednisolone or betamethasone or cortison* or deflazacort or calcort or dexamethasone or hydrocortisone or efcortisol or hydrocortone or solu-cortef or methylprednisolone or solu-medrone or depo-medrone or triamcinolone or kenalog)

S5 (MM "Hydrocortisone") or (MM "Prednisolone") or (MM "Betamethasone") or (MM "Cortisone") or (MM "Antiinflammatory Agents") or (MH "Immunosuppressive Agents+") or (MH "Glucocorticoids") or (MM "Dexamethasone") or (MM "Steroids") or (MM "Methylprednisolone") or (MM "Triamcinolone") or (MH "Drug Hypersensitivity+")

S6 S4 or S5

S7 S3 and S6

S8 TX random* or trial* or multicenter* or ((double or single or triple) and (mask* or blind*)) or placebo*

S9 S7 and S8

WHAT'S NEW

Date	Event	Description
14 December 2018	Amended	Editorial team changed to Cochrane Emergency and Critical Care
18 June 2014	Review declared as stable	This Cochrane review has been marked as 'stable no longer being updated' as there are no randomized controlled trials (RCTs) and for ethical reasons there are unlikely to be any RCTs in the future. If the situation changes, then the authors will update the review.

HISTORY

Protocol first published: Issue 1, 2009

Review first published: Issue 3, 2010

Date	Event	Description
29 January 2016	Amended	Lead author's contact details updated
11 July 2012	Amended	Contact details updated.
31 May 2012	Amended	Contact details updated.
17 April 2012	Amended	Contact details updated.
6 February 2012	New search has been performed	We updated the methods section.
6 February 2012	New citation required but conclusions have not changed	In the previous version of our review (Choo 2010) we ran the database searches until September 2009. In this version we re-ran the database searches until September 2011. We found no new studies that fitted our inclusion criteria.
31 August 2010	Amended	Contact details updated.
17 March 2010	Amended	Aziz Sheikh's affiliation updated. Acknowledgement section corrected.
8 January 2009	Amended	1. Minor edits made to text: correcting typos and inserting three new references in background section: Gupta 2003 ; Gupta 2007 ; Sheikh 2008 . 2. Order of authors for citation amended. Previously: Sheikh, Simons, Choo; now reads: Choo, Simons, Sheikh

CONTRIBUTIONS OF AUTHORS

Conceiving the review: Aziz Sheikh (AS) and Estelle Simons (ES)
Co-ordinating the review: Karen Choo (KC)
Undertaking manual searches: KC
Screening search results: KC and AS
Organizing retrieval of papers: KC
Screening retrieved papers against inclusion criteria: KC and AS
Appraising quality of papers: there were no eligible studies
Abstracting data from papers: there were no eligible studies
Writing to authors of papers for additional information: there were no eligible studies
Providing additional data about papers: there were no eligible studies
Obtaining and screening data on unpublished studies: KC and AS
Data management for the review: KC and AS
Entering data into Review Manager ([RevMan 5.1](#)): KC
RevMan statistical data: there were no eligible studies
Other statistical analysis not using RevMan: there were no eligible studies
Double entry of data: there were no eligible studies

Interpretation of data: there were no eligible studies
Statistical inferences: there were no eligible studies
Writing the review: KC, AS, and ES
Securing funding for the review: AS
Performing previous work that was the foundation of the present study: AS and ES
Guarantor for the review (one author): AS
Person responsible for reading and checking review before submission: KC, AS and ES

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- Allergy & Respiratory Research Group, Centre for Population Health Sciences, The University of Edinburgh, UK.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We amended the [Types of participants](#) section slightly by including the following additional inclusion criteria: biologics, anaesthetics, exercise, as well as idiopathic disease.

In November 2011 we updated the risk of bias tool.

INDEX TERMS

Medical Subject Headings (MeSH)

Anaphylaxis [*drug therapy]; Glucocorticoids [*therapeutic use]

MeSH check words

Humans