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[Intervention Review]

Different oral corticosteroid regimens for acute asthma

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ABSTRACT

Background

Asthma is a common long-term breathing condition that affects approximately 300 million people worldwide. People with asthma may experience short-term worsening of their asthma symptoms; these episodes are often known as 'exacerbations', 'flare-ups', 'attacks' or 'acute asthma'. Oral steroids, which have a potent anti-inflammatory effect, are recommended for all but the most mild asthma exacerbations; they should be initiated promptly. The most often prescribed oral steroids are prednisolone and dexamethasone, but current guidelines on dosing vary between countries, and often among different guideline producers within the same country. Despite their proven efficacy, use of steroids needs to be balanced against their potential to cause important adverse events. Evidence is somewhat limited regarding optimal dosing of oral steroids for asthma exacerbations to maximise recovery while minimising potential side effects, which is the topic of this review.

Objectives

To assess the efficacy and safety of any dose or duration of oral steroids versus any other dose or duration of oral steroids for adults and children with an asthma exacerbation.

Search methods

We identified trials from the Cochrane Airways Group Specialised Register (CAGR), ClinicalTrials.gov (www.ClinicalTrials.gov), the World Health Organization (WHO) trials portal (www.who.int/ictrp/en/) and reference lists of all primary studies and review articles. This search was up to date as of April 2016.

Selection criteria

We included parallel randomised controlled trials (RCTs), irrespective of blinding or duration, that evaluated one dose or duration of oral steroid versus any other dose or duration, for management of asthma exacerbations. We included studies involving both adults and children with asthma of any severity, in which investigators analysed adults and children separately. We allowed any other co-intervention in the management of an asthma exacerbation, provided it was not part of the randomised treatment. We included studies reported as full text, those published as abstract only and unpublished data.

Data collection and analysis

Two review authors independently screened the search results for included trials, extracted numerical data and assessed risk of bias; all data were cross-checked for accuracy. We resolved disagreements by discussion with the third review author or with an external advisor.

We analysed dichotomous data as odds ratios (ORs) or risk differences (RDs) using study participants as the unit of analysis; we analysed continuous data as mean differences (MDs). We used a random-effects model, and we carried out a fixed-effect analysis if we detected



statistical heterogeneity. We rated all outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) system and presented results in 'Summary of findings' tables.

Main results

We included 18 studies that randomised a total of 2438 participants - both adults and children - and performed comparisons of interest. Included studies assessed higher versus lower doses of prednisolone (n = 4); longer versus shorter courses of prednisolone (n = 3) or dexamethasone (n = 1); tapered versus non-tapered courses of prednisolone (n = 4); and prednisolone versus dexamethasone (n = 6). Follow-up duration ranged from seven days to six months. The smallest study randomised just 15 participants, and the largest 638 (median 93). The varied interventions and outcomes reported limited the number of meaningful meta-analyses that we could perform.

For two of our primary outcomes - hospital admission and serious adverse events - events were too infrequent to permit conclusions about the superiority of one treatment over the other, or their equivalence. Researchers in the included studies reported asthma symptoms in different ways and rarely used validated scales, again limiting our conclusions. Secondary outcome meta-analysis was similarly hampered by heterogeneity among interventions and outcome measures used. Overall, we found no convincing evidence of differences in outcomes between a higher dose or longer course and a lower dose or shorter course of prednisolone or dexamethasone, or between prednisolone and dexamethasone.

Included studies were generally of reasonable methodological quality. Review authors assessed most outcomes in the review as having low or very low quality, meaning we are not confident in the effect estimates. The predominant reason for downgrading was imprecision, but indirectness and risk of bias also reduced our confidence in some estimates.

Authors' conclusions

Evidence is not strong enough to reveal whether shorter or lower-dose regimens are generally less effective than longer or higher-dose regimens, or indeed that the latter are associated with more adverse events. Any changes recommended for current practice should be supported by data from larger, well-designed trials. Varied study design and outcome measures limited the number of meta-analyses that we could perform. Greater emphasis on palatability and on whether some regimens might be easier to adhere to than others could better inform clinical decisions for individual patients.

PLAIN LANGUAGE SUMMARY

Different doses and durations of oral steroids for asthma attacks

Background: People with asthma sometimes have asthma attacks, wherein their symptoms such as cough, chest tightness and difficulty breathing become worse. Many patients with asthma attacks are treated with steroids, which are usually given as a short course of tablets or liquid medicine. Steroids work by reducing inflammation in the airways in the lungs, but they can have side effects (e.g. reduced growth in children, hyperactivity, nausea).

Review question: We set out to compare different doses or durations of oral steroids given to people having asthma attacks. This is an important issue because different doses and durations of oral steroids are used for asthma attacks in different countries, and we do not know which regimen is most likely to improve symptoms while minimising unpleasant side effects.

Study characteristics: We included 18 studies involving 2438 adults and children. Studies compared two types of steroid - prednisolone and dexamethasone - or two different doses or durations of either drug. The smallest study included just 15 people, and the largest 638. Studies followed people for between seven days and six months to see what happened to them. The evidence presented here is current to April 2016.

Key results: It was difficult to combine the results of studies in a useful way because investigators used a variety of doses and durations of steroids and measured their results in different ways. Also, events such as hospital admissions and serious side effects happened very rarely in these studies, making it difficult to tell whether longer or shorter courses or higher or lower doses are better or safer, or if prednisolone is generally better or worse than dexamethasone. Some studies were old and did not use steroid doses or durations used by medical practitioners today.

Any changes to the way in which asthma attacks are currently managed with oral steroids would need to be supported by larger studies than have been conducted so far.

Quality of the evidence: Evidence presented in this review is generally considered to be of low or very low quality, which means we are not very sure whether the results are accurate, mostly because we have not been able to combine many studies. Some studies did not clearly explain how trial organisers decided which people would receive which dose of steroids, and in some studies, both participants and trial organisers knew which dose they were getting. This may have affected study results.