

# EVIDENCE-BASED HEALTH CARE

## INHALED CORTICOSTEROIDS FOR NON-SPECIFIC COUGH IN CHILDREN

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### Background

You see a 5-year-old child with a chronic cough, and no other evidence of asthma or other chronic chest condition. Her mother is concerned about the cough and mentions a friend of the child with a similar problem who was given inhaled steroids, and improved. She has however also heard that inhaled steroids have side-effects. You have recently attended a short course on evidence-based practice and you decide to hone your new-found skills by checking the evidence.

### So what is the question?

One question might be: 'In children with a chronic cough and no clear cause, how effective are inhaled corticosteroids in reducing the frequency of the cough?' (Note that the question specifies the type of person, intervention and outcome that interest you.)

### The type of evidence to look for, and where to look for it

You know that treatments are best assessed by randomised controlled trials (RCTs),\* and the best evidence of all, if available, usually comes from a systematic review\* of valid randomised controlled trials. You have access to the Cochrane Library,\* and decide to check that first.

#### Aims

This feature on evidence-based health care aims to present useful practice-related information on topics relevant to readers of *Current Allergy & Clinical Immunology*. The treatment of each topic is not comprehensive. The main aim is to illustrate selected aspects of the process of i) getting the evidence straight and ii) applying valid evidence to practice. The box entitled 'Some terms explained' enlarges on the technical terms mentioned in the text and marked with an asterisk (\*).

### What was found

You find a Cochrane systematic review of inhaled corticosteroids for non-specific cough in children aged over 2 years.<sup>1</sup> It was last updated in August 2005.

### Results

The review identified only two trials involving 123 participants. One examined beclomethasone 400 µg per day,<sup>2</sup> and the other fluticasone 2 000 µg daily for 3 days, followed by 1 000 µg daily for 11 days.<sup>3</sup> The main findings, compared with placebo, were:

Outcome	Steroid	Placebo	Difference in means	95% CI
<i>Beclomethasone 400 µg/day<sup>2</sup></i>	<i>n=18</i>	<i>n=20</i>		
% change in cough frequency per day (measured by a validated electronic cough meter)	-72.0%	-45.0%	-27.0%	-83 to 29%
			<b>RR</b>	<b>95% CI</b>
<i>Fluticasone high dose<sup>3</sup></i>				
75% improvement in cough frequency (measured by a video and auditory recording system)	17/24	8/23	2.04	1.10 to 3.8

CI – confidence interval, RR – relative risk

### Some comments

With low-dose inhaled steroids the point estimate ('best guess') is that the reduction of the frequency of cough was greater in the steroid group by 27%. However the trial was small, which increases the probability that this difference is due to chance. The 95% confidence interval\* of -83 to 29% indicates that the true difference could plausibly be anywhere between a reduction of 83% or an increase of 29%. This offers no evidence that it is either effective or ineffective.

Given high-dose steroids, 71% of children had improved by at least 75% after 15-18 days. However 35% of the placebo group had also improved! The chance ('risk') of such improvement was thus about 2 times higher in the treated group (71%/35%). Another way of saying this is that the relative risk (RR)\* for improvement was 2. The 95% confidence interval for the RR (1.10 to 3.8) indicates that the chance ('risk') of improvement on steroids could plausibly be anywhere between 1.10 and 3.8 times that on placebo.

It is interesting that the cough frequency of one-third of the children on placebo also improved by at least 75%. This illustrates the need for a control group, because many factors in addition to inhaled steroids can result in improvement. (In this case it could be because, in chronic fluctuating conditions such as asthma, one's worst days or weeks are very likely to be followed by improvement. Most additions to treatment take place during the 'bad' phase, i.e. at a time when some

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improvement is likely to take place soon in the natural course of events. Beware of automatically attributing improvement in chronic relapsing conditions to a new treatment.)

The child's mother was worried about the side-effects of inhaled steroids. From this study, three children needed exposure to high-dose inhaled steroids for one to benefit. Is the benefit to one child worth the risk to three? That depends on the adverse effects of the treatment, which the review does not address and the included trials do not report. It is a problem that many trials, and systematic reviews of trials, pay little attention to adverse effects. RCTs are usually designed to detect benefits. Potentially clinically important adverse effects are often not measured, or trials are too small or follow-up is too short to detect rare but important harmful effects. (That is why postmarketing surveillance is so important.) A major concern about high-dose inhaled steroids in children is the effect on growth. Another Cochrane Review has found that a standard dose of beclomethasone 400 µg/day caused an average decrease in linear growth of -1.54 cm/year, although this could conceivably reverse with 'catch up' growth after stopping treatment.<sup>4</sup>

Should you give your patient high-dose inhaled steroids or not? As with many choices in clinical practice the available evidence does not give a clear answer. This is

partly because there is insufficient evidence, but also because the decision involves balancing expected benefits against possible harms. The balance depends on many factors, including how averse the patient (or parents) are to taking risks, and the value they place respectively on avoidance of the cough and the adverse effects. For many people, the risks of high-dose inhaled steroids would outweigh the relatively small beneficial effect on the cough.

## REFERENCES

1. Tomerak AAT, McGlashan JJM, Lakhanpaul M, Vyas HHV, McKean MC. Inhaled corticosteroids for non-specific chronic cough in children. *The Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD004231.pub2. DOI: 10.1002/14651858.CD004231.pub2.
2. Chang AB, Phelan PD, Carlin JB, Sawyer SM, Robertson CF. A randomised, placebo controlled trial of inhaled salbutamol and beclomethasone for recurrent cough. *Arch Dis Child* 1998; **79**: 6-11.
3. Davies M, Fuller P, Picciotto A, McKenzie SA. Persistent nocturnal cough: randomised controlled trial of high dose inhaled corticosteroid. *Arch Dis Child* 1999; **81**: 38-44.
4. Sharek PJ, Bergman DA, Ducharme F. Beclomethasone for asthma in children: effects on linear growth. *The Cochrane Database of Systematic Reviews* 1999, Issue 3. Art. No.: CD001282. DOI: 10.1002/14651858.CD001282

### \*Some terms explained

**Confidence interval.** Although not the strictly correct definition, for practical purposes a 95% confidence interval indicates the range within which the true size of the effect is likely to fall. As an example, in the Chang study, the point estimate ('best guess') was a 27% greater reduction of the frequency of cough in the steroid group. However this point estimate might not be spot on, by chance alone, because of the small numbers in the study. The true effect could plausibly be anywhere between a reduction of 83% or an increase of 29%.

**Relative risk (risk ratio)** is the ratio of the risk of an outcome in the treated group to the risk in the control group. A relative risk of 1 means that the risk of the outcome is the same in both groups, i.e. the treatment has no effect. A relative risk below 1 means that the intervention reduces the risk of the outcome. Above 1 means increased risk. A relative risk below 1 for a bad outcome is thus a good thing, but for a good outcome (e.g. recovery) it means the treatment did harm (by reducing the 'risk' of recovery).

**Randomised controlled trial.** In a controlled trial patients are actively allocated to either receive treatment or be in a control group. The control group allows comparison of the treatment with the outcome without treatment. However the two

groups need to be as similar as possible before the trial starts, so that any differences at the end can be attributed to the treatment. Randomly allocating participants to treatment or control is the best way we know of ensuring that the groups are comparable.

**Systematic review.** This is a literature review conducted itself like a research study, in order to minimise the many unintended (and sometimes subtle) biases that can creep into traditional literature reviews. It uses specified systematic methods to identify, appraise and summarise studies aimed at answering a defined question. A Cochrane review is a systematic review performed under the auspices of an international collaboration called the Cochrane Collaboration. (One advantage of Cochrane systematic reviews is that they are regularly updated. A new electronic version of the Library is published every three months, and individual reviews are updated regularly.) There are however many systematic reviews performed outside of the Cochrane Collaboration.

**The Cochrane Library** is an electronic collection of over 2 000 high-quality systematic reviews, and is a good first port of call when looking for evidence on interventions. Abstracts of Cochrane Reviews are available free of charge at <http://www.thecochranelibrary.com>