Cochrane Library

Cochrane Database of Systematic Reviews

Inhaled corticosteroids for cystic fibrosis (Review)

Balfour-Lynn IM, Welch K, Smith S

Balfour-Lynn IM, Welch K, Smith S.
Inhaled corticosteroids for cystic fibrosis.
Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD001915.
DOI: 10.1002/14651858.CD001915.pub6.

www.cochranelibrary.com

WILEY

[Intervention Review]

Inhaled corticosteroids for cystic fibrosis

Ian M Balfour-Lynn[1], Karen Welch[2], Sherie Smith[3]

[1]Dept. Paediatric Respiratory Medicine, Royal Brompton Hospital, London, UK. [2]c/o Cochrane Cystic Fibrosis and Genetic Disorders Review Group, University of Liverpool, Institute in the Park, Liverpool, UK. [3]Division of Child Health, Obstetrics & Gynaecology (COG), School of Medicine, University of Nottingham, Nottingham, UK

Contact address: Ian M Balfour-Lynn, Dept. Paediatric Respiratory Medicine, Royal Brompton Hospital, Sydney Street, London, SW3 6NP, UK. i.balfourlynn@ic.ac.uk.

Editorial group: Cochrane Cystic Fibrosis and Genetic Disorders Group
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 7, 2019.

Citation: Balfour-Lynn IM, Welch K, Smith S. Inhaled corticosteroids for cystic fibrosis. *Cochrane Database of Systematic Reviews* 2019, Issue 7. Art. No.: CD001915. DOI: 10.1002/14651858.CD001915.pub6.

ABSTRACT

Background

The reduction of lung inflammation is one of the goals of cystic fibrosis therapy. Inhaled corticosteroids are often used in this respect to treat children and adults with cystic fibrosis. The rationale for this is their potential to reduce lung damage arising from inflammation, as well as their effect on symptomatic wheezing. It is important to establish the current level of evidence for the risks and benefits of inhaled corticosteroids, especially in the light of their known adverse effects on growth. This is an update of a previously published review; however, due to the lack of research in this area, we do not envisage undertaking any further updates.

Objectives

To assess the effectiveness of taking regular inhaled corticosteroids compared to not taking them in children and adults with cystic fibrosis.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register, comprising references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings. We requested information from pharmaceutical companies manufacturing inhaled corticosteroids and authors of identified trials.

Date of most recent search of the Group's Trials Register: 19 November 2018.

Selection criteria

Randomised or quasi-randomised trials, published and unpublished, comparing inhaled corticosteroids to placebo or standard treatment in individuals with cystic fibrosis.

Data collection and analysis

Two independent authors assessed methodological quality and risk of bias in trials using established criteria and extracted data using standard pro formas. The quality of the evidence was assessed using the GRADE criteria.

Main results

The searches identified 35 citations, of which 27 (representing 13 trials) were eligible for inclusion. These 13 trials reported the use of inhaled corticosteroids in 525 people with cystic fibrosis aged between 6 and 55 years. One was a withdrawal trial in 171 individuals who were already taking inhaled corticosteroids. Methodological quality and risk of bias were difficult to assess from published information.

Objective measures of airway function were reported in most trials but were often incomplete and reported at different time points. We found no difference in forced expiratory volume in one second (FEV_1) or forced vital capacity (FVC) % predicted in any of the trials, although the quality of the evidence was low due to risks of bias within the included trials and low participant numbers. We are uncertain whether inhaled corticosteroids result in an improvement in exercise tolerance, bronchial hyperreactivity or exacerbations as the quality of the evidence was very low. Data from one trial suggested that inhaled corticosteroids may make little or no difference to quality of life (low-quality evidence).

Three trials reported adverse effects, but the quality of the evidence is low and so we are uncertain whether inhaled corticosteroids increase the risk of adverse effects. However, one study did show that growth was adversely affected by high doses of inhaled corticosteroids.

Authors' conclusions

Evidence from these trials is of low to very low quality and insufficient to establish whether inhaled corticosteroids are beneficial in cystic fibrosis, but withdrawal in those already taking them has been shown to be safe. There is some evidence they may cause harm in terms of growth. It has not been established whether long-term use is beneficial in reducing lung inflammation, which should improve survival, but it is unlikely this will be proven conclusively in a randomised controlled trial.

PLAIN LANGUAGE SUMMARY

Inhaled corticosteroids for cystic fibrosis

Review question

We reviewed the evidence about the effect of inhaled corticosteroids in people with cystic fibrosis.

Background

Repeated chest infections in people with cystic fibrosis cause inflammation and damage to the lungs which, in the long term, is the most common reason for death. Inhaled corticosteroids are often used to treat inflammation, but may cause some side effects. Some of these side effects are less serious, e.g., oral thrush, but others are more serious, such as reduced growth rate in childhood. This is an update of a previously published review and due to a lack of research in this area, we do not plan any further updates.

Search date

The last search for evidence was on 19 November 2018.

Study characteristics

In this updated review, 13 trials reported the use of inhaled corticosteroids in 525 people with cystic fibrosis. In most of the trials participants started taking steroids or placebo (treatment that appeared the same as the steroids, but did not have any active medicine in it) at the start of the trial, but one trial was a withdrawal trial (171 participants), where everyone was already taking steroids and while half of them carried on, the rest took a placebo, in effect stopping the treatment. Participants were aged between 6 and 55 years; three of the trials were in children only, four in adults only and four were mixed ages; two trials did not describe the ages of the people taking part. The lung function and severity of disease of the participants varied across trials and only two trials gave information about their genetic mutations. All trials took place in Europe. In 10 of the trials, all those taking part remained in the same group up to the end of the trial (either a treatment group or a group receiving no treatment or a placebo), but in three trials they swapped groups halfway through the trial. The trials lasted between three weeks and two years.

Key results

The clinical trials have not been able to prove that inhaled corticosteroids reduce inflammation in the lungs of people with cystic fibrosis. We found no difference in measurements of lung function, exercise tolerance, the reaction of airways to irritation or the number of exacerbations (flare up of symptoms). Generally, it was unclear if inhaled corticosteroids increased the risk of adverse effects, but one trial did show that these drugs can slow down children's growth when used in high doses. Furthermore, results from the withdrawal trial showed that under close supervision of the cystic fibrosis team, it may be safe for people who have been taking inhaled corticosteroids for some time to stop doing so.

Quality of the evidence

We thought the quality of the evidence was low to very low. A lack of information meant we were often not able to judge if the way the trials were designed or run could have affected our confidence in the results. Only three trials gave details of how they made sure people taking part had equal chances of being in the treatment or placebo groups; and only five described how they made sure the people recruiting participants did not know which groups they would be going into. In most cases, we did not think that once the trials started the people taking part or their doctors knew whether they were getting steroids or placebo. However, we did have some concerns that four of the

trials had not been published in journals, who would have sent the reports to experts to check for accuracy and we were not sure how this might affect our confidence in the results.