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[Intervention Review]

Oral non-steroidal anti-inflammatory drug therapy for lung disease in cystic fibrosis

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ABSTRACT

Background

Progressive lung damage causes most deaths in cystic fibrosis. Non-steroidal anti-inflammatory drugs (such as ibuprofen) may prevent progressive pulmonary deterioration and morbidity in cystic fibrosis.

Objectives

To assess the effectiveness of treatment with non-steroidal anti-inflammatory drugs in cystic fibrosis.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register comprising references identified from comprehensive electronic database searches, hand searches of relevant journals and abstract books of conference proceedings. We contacted manufacturers of non-steroidal anti-inflammatory drugs.

Latest search of the Group's Trials Register: 04 February 2016.

Selection criteria

Randomized controlled trials comparing oral non-steroidal anti-inflammatory drugs, at any dose for at least two months, to placebo in people with cystic fibrosis.

Data collection and analysis

Two authors independently assessed trials for inclusion the review and their potential risk of bias.

Main results

The searches identified 10 trials; four are included (287 participants aged five to 39 years; maximum follow up of four years) and one is currently awaiting classification pending publication of the full trial report. Three trials compared ibuprofen to placebo (two from the same centre with some of the same participants); one trial assessed piroxicam versus placebo.

The three ibuprofen trials were deemed to have good or adequate methodological quality, but used various outcomes and summary measures. Reviewers considered measures of lung function, nutritional status, radiological assessment of pulmonary involvement, intravenous antibiotic usage, hospital admissions, survival and adverse effects. Combined data from the two largest ibuprofen trials showed a significantly lower annual rate of decline for lung function, percent predicted forced expiratory volume in one second mean

difference 1.32 (95% confidence interval 0.21 to 2.42); forced vital capacity mean difference 1.27 (95% confidence interval 0.26 to 2.28); forced expiratory flow (25-75%) mean difference 1.80 (95% confidence interval 0.15 to 3.45). The post-hoc analysis of data from two trials split by age showed a statistically significant slower rate of annual decline of percent predicted forced expiratory volume in one second and forced vital capacity in the ibuprofen group in younger children, mean difference 1.41% (95% confidence interval 0.03 to 2.80) and mean difference 1.32% (95% confidence interval 0.04 to 2.60) respectively. In one trial, long-term use of high-dose ibuprofen was associated with reduced intravenous antibiotic usage, improved nutritional and radiological pulmonary status. No major adverse effects were reported, but the power of the trials to identify clinically important differences in the incidence of adverse effects was low.

We did not have any concerns with regards to risk of bias for the trial comparing piroxicam to placebo. However, the trial did not report many data in a form that we could analyse in this review. No data were available for the review's primary outcome of lung function; available data for hospital admissions showed no difference between the groups. No analysable data were available for any other review outcome.

Authors' conclusions

High-dose ibuprofen can slow the progression of lung disease in people with cystic fibrosis, especially in children, which suggests that strategies to modulate lung inflammation can be beneficial for people with cystic fibrosis.

PLAIN LANGUAGE SUMMARY

Treatment with oral drugs other than steroids to reduce lung inflammation and deterioration in lung function in people with cystic fibrosis

Review question

We reviewed evidence to see if drugs that weren't steroids could reduce inflammation in the lungs and stop lung function getting worse in people with cystic fibrosis.

Background

Inflammation in the lungs increases the damage done to them and is the most common reason for early death in people with cystic fibrosis. In high doses, non-steroidal anti-inflammatory drugs, particularly ibuprofen, may work against inflammation, but in low doses there is some evidence that they may cause the inflammation. The use of high doses has also raised concerns about the potential for unwanted effects, which has limited the use of these drugs in cystic fibrosis.

Search date

The evidence is current to: 04 February 2016.

Study characteristics

We looked for trials comparing oral non-steroidal anti-inflammatory drugs to a a placebo (a tablet that contained no active medicine). We looked for any dose level. but the trial had to run for at least two months in people with cystic fibrosis. We found 10 trials and included four of these with a total of 287 people aged five to 39 years; one trial has not yet been published in full and we will assess this when we have more information. Three of the included trials compared ibuprofen to a placebo; two of these trials were run in the same centre and used some of the same people. One trial compared a drug called piroxicam to placebo. The longest trial lasted four years.

We aimed to report on lung function, nutritional status, lung x-rays, how often intravenous antibiotics were needed, details about hospital admissions, survival and side effects.

Key results

We could combined data from the two largest ibuprofen trials and showed that volunteers taking ibuprofen had a significantly lower annual rate of decline in lung function which was consistent across three different ways of measuring the outcome. We then decided to look at these results split by age (even though we did not originally plan to do this) and found that two of the lung function measurements showed a statistically significant slower rate of annual decline in lung function in younger children. In one trial, long-term use of a high dose of ibuprofen was linked to less need for intravenous antibiotics, better nutritional status and healthier lungs as seen by x-ray. No major side effects were reported in the trials, but they had not been designed to show differences in the rates of side effects.

To summarise, we found evidence showing that a high dose of a non-steroidal anti-inflammatory drug, most notably ibuprofen, can slow the progression of lung damage in people with cystic fibrosis, especially in younger people. The long-term safety data are limited but we feel that there is enough evidence to recommend that non-steroidal anti-inflammatory drugs be temporarily stopped when people with cystic fibrosis are receiving intravenous aminoglycosides or other drugs that may badly damage the kidneys.

The piroxicam trial did not report many results in a form that we could analyse in the review. We did not have any results for our main outcome of lung lung function. The only results we had reported no difference between the piroxicam group and the placebo group for the number of hospital admissions.

Quality of the evidence

We thought the three ibuprofen trials had a good or adequate level of methodological quality with little risk of bias to the results, but used a range of different outcomes and summary measures. We did not have any concerns with regards to risks of bias for the trial comparing piroxicam to placebo.