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[Intervention Review]

Interventions for preventing distal intestinal obstruction syndrome (DIOS) in cystic fibrosis

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ABSTRACT

Background

Cystic fibrosis (CF) is the most common, life-limiting, genetically inherited disease. It affects multiple organs, particularly the respiratory system. However, gastrointestinal problems such as constipation and distal intestinal obstruction syndrome (DIOS) are also important and well-recognised complications in CF. They share similar symptoms e.g. bloating, abdominal pain, but are distinct conditions. Constipation occurs when there is gradual faecal impaction of the colon, but DIOS occurs when there is an accumulation of faeces and sticky mucus, forming a mass in the distal part of the small intestine. The mass may partially block the intestine (incomplete DIOS) or completely block the intestine (complete DIOS). Symptoms of DIOS can affect quality of life and other aspects of CF health, such as airway clearance, exercise, sleep and nutritional status. Treatment of constipation and prevention of complete bowel obstruction are required for gastrointestinal management in CF. However, many different strategies are used in clinical practice and there is a lack of consensus. The importance of this topic was highlighted in a recent research priority setting exercise by the James Lind Alliance.

Objectives

To evaluate the effectiveness and safety of laxative agents of differing types for preventing DIOS (complete and incomplete) in children and adults with CF.

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. Date of search: 22 May 2018.

We also searched online trial registries. Date of last search: 10 June 2018.

Selection criteria

Randomised and quasi-randomised controlled parallel trials comparing laxative therapy for preventing DIOS (including osmotic agents, stimulants, mucolytics and substances with more than one action) at any dose to placebo, no treatment or an alternative laxative therapy, in people of any age with pancreatic sufficient or insufficient CF and any stage of lung disease. Randomised cross-over trials were judged on an individual basis.

Data collection and analysis

Two authors independently assessed trials for inclusion, extracted outcome data and performed a risk of bias assessment for the included data. We judged the quality of the evidence using GRADE criteria.

Main results

We included one cross-over trial (17 participants) with a duration of 12 months, in which participants were randomly allocated to either cisapride (a gastro-prokinetic agent) or placebo for six months each. The trial had an unclear risk of bias for most domains but had a high risk of reporting bias.

Radiograph scores revealed no difference in occurrence of DIOS between cisapride and placebo (narrative report, no data provided). There were no adverse effects. Symptom scores were the only secondary outcome within the review that were reported. Total gastrointestinal symptom scores favoured cisapride with a statistically significant mean difference (MD) of -7.60 (95% confidence interval (CI) -14.73 to -0.47). There was no significant difference at six months between cisapride and placebo for abdominal distension, MD -0.90 (95% CI -2.39 to 0.59) or abdominal pain, MD -0.4 (95% CI -2.05 to 1.25). The global symptom scores (whether individuals felt better or worse) were reported in the paper to favour cisapride and be statistically significant ($P < 0.05$).

We assessed the available data to be very low quality. There was a great deal of missing data from the included trial and the investigators failed to report numerical data for many outcomes. The overall risk of bias of the trial was unclear and it had a high risk for reporting bias. There was also indirectness; the trial drug (cisapride) has since been removed from the market in several countries due to adverse effects, thus it has no current applicability for preventing DIOS. The included trial also had very few participants, which downgraded the quality a further level for precision.

Authors' conclusions

There is an absence of evidence for interventions for the prevention of DIOS. As there was only one included trial, we could not perform a meta-analysis of the data. Furthermore, the included trial compared a prokinetic agent (cisapride) that is no longer licensed for use in a number of countries due to the risk of serious cardiac events, a finding that came to light after the trial was conducted. Therefore, the limited findings from the trial are not applicable in current clinical practice.

Overall, a great deal more research needs to be undertaken on gastrointestinal complications in CF, as this is a very poorly studied area compared to respiratory complications in CF.

PLAIN LANGUAGE SUMMARY

Which interventions are effective and safe for preventing distal intestinal obstruction syndrome (DIOS) in cystic fibrosis?

Background

Cystic fibrosis (CF) is an inherited, life-long condition that causes organ systems in the body to produce large amounts of thick and sticky mucus. The most commonly affected area is the lungs, in which thick mucus leads to recurrent chest infections and breathing difficulties. Another commonly affected area is the digestive system. Many people with CF suffer from bloating and abdominal pain which may be caused by constipation or distal intestinal obstruction syndrome (DIOS). In DIOS, overproduction of thick mucus combines with stool and sticks to the intestinal wall. This mass can partially block the intestine (incomplete DIOS) or completely block the intestine (complete DIOS). The latter causes severe pain, vomiting and is treated as a medical emergency. As part of effective care for people with CF, constipation should therefore be treated and complete bowel obstruction be prevented. It is also important to recognise that constipation and DIOS impact on other aspects of CF health. Bloating, abdominal pain and nausea may affect airway clearance, exercise and sleep. Nutritional status may also be affected due to decreased appetite and malabsorption. DIOS may affect the absorption of other medications taken by people with CF. Overall, DIOS can significantly impair quality of life. Different laxatives are currently used in clinics, but prescribing practices differ and there is no consensus on optimal treatment strategies. Hence, this review aimed to analyse the evidence for the preventing DIOS.

Search date

We last searched for evidence: 10 June 2018.

Trial characteristics

We included one trial in the review, which included 17 people aged between 13 to 35 years. These people were randomly put into groups to take either a placebo drug (with no active medication) or cisapride for six months each and then to cross over and take the alternative treatment for a further six months.

Key results

The trial used radiography to diagnose DIOS, but did not provide any data and only stated that there was no difference between cisapride and placebo. The trial also stated that there were no adverse effects from the cisapride. The trial assessed participant-reported total and

individual gastrointestinal symptom scores. People in the cisapride group reported an improvement in total gastrointestinal symptom scores compared to those in the placebo group. However, there were no differences reported between groups for the individual symptom scores of abdominal pain and abdominal distension (swelling). Participants also reported global symptom scores, which showed that most people felt better taking cisapride compared to placebo.

Quality of the evidence

The overall quality of the evidence was very low. With one trial in this review, we could not combine data from different trials. The trial did not provide enough information about the methods used for allocating participants or about missing data and did not fully report certain results. The small number of participants also lowered the precision of the results. Since this trial was conducted, cisapride has been removed from the market in a number of countries due to rare but serious heart complications, therefore it has no applicability to current clinical practice.