

Lansoprazole for children with poorly controlled asthma

Design: Randomised placebo-controlled trial (RCT).

Allocation: 1:1 ratio of intervention:placebo using permuted-block assignment stratified by clinical centre.

Setting: 19 American Lung Association Asthma Clinical Research Center sites from April 2007 to April 2011.

Patients: Children aged 6–17 years (mean 11 years) with physician and lung function confirmed poorly controlled asthma, all of whom had been treated with inhaled corticosteroids for at least 8 weeks prior to enrolment. Patients with current or previous gastro-oesophageal reflux disease requiring treatment were excluded. A subgroup of 115 received pH studies.

Intervention: 149 children received lansoprazole (15 mg/day <30 kg or 30 mg/day >30 kg) and 157 received placebo.

Outcomes: Primary outcome—Change in Asthma Control Questionnaire (ACQ) score. Secondary outcomes—Rate of episodes of acute asthma, asthma symptom utility index, asthma control test for adolescents, asthma-specific quality of life for children score, meaningful clinically important changes in lung function tests, gastrointestinal symptoms or nocturnal awakenings.

Follow-up period: 24 weeks.

Patient follow-up: 132/149 of those randomised to lansoprazole and 131/157 to placebo group. All patients were included in the intention-to-treat analysis. Self-reported adherence was >90% in both groups.

Main results: ACQ score decreased by a less than clinically important amount in both groups (mean 0.2 units (95% CI 0.0 to 0.3 units). There was no significant difference between treatment groups for all primary and secondary outcomes. 43% of pH studies revealed GOR but there was no difference in outcome measures for those testing positive and receiving lansoprazole compared to placebo.

There was an increased risk of upper respiratory tract infection (URTI) (RR 1.3 (95% CI 1.1 to 1.6) (p=0.02)), sore throat (RR 1.3 (5% CI 1.0 to 1.6) (p=0.02)) and bronchitis (RR 2.2 (95% CI 0.8 to 6.1) (p=0.04)) among the intervention group.

Conclusion: Lansoprazole does not improve symptoms, quality of life or lung function measures in children with poorly controlled asthma asymptomatic of GOR. Its use may be associated with an increased risk of respiratory infection.

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Gastro-oesophageal reflux (GOR) and asthma are common medical conditions which often co-exist. The incidence of GOR has been found to be up to 75% in children with problematic severe asthma.^{1–2} It may be that they concur coincidentally, that reflux worsens the asthma or that the asthma causes reflux. It would seem logical that GOR worsens asthma control because we know that GOR can cause wheeze. Early paediatric case-control studies suggested that treatment of GOR improve asthma symptoms and reduce exacerbations.² However, only one RCT has been performed in asthmatic children symptomatic of GOR and this did not show improvement in asthma symptoms or lung function.³ There was a suggestion of maybe some benefit in those with severe GOR. A Cochrane review of adults and children concluded no improvement in asthma following treatment for GOR, but noted there was little paediatric data.⁴

However, the question remains unanswered; should we treat GOR in a child with asthma asymptomatic of GOR? The present study is the first to eloquently investigate this in mild-moderate patients with poor asthma control. Interestingly, it showed no improvement in symptoms, quality of life or lung function but it actually showed that the addition of lansoprazole was associated with a greater incidence of URTI and bronchitis, so may cause harm. It may be

that the addition of lansoprazole will result in the reduction of gastric acid, which may in turn affect host defence to bacterial colonisation.⁵

There were unavoidable limitations of the study; first, it should be interpreted in the patient group selected and not extrapolated to problematic severe asthma. Second, compliance was self-reported and thus not assured and doses were not tailored to effectiveness of treatment. Lastly, URTIs were self-reported and not proven. A larger RCT inclusive of a group of patients with severe asthma and concurrent severe GOR with viral PCR and pH studies on treatment would be informative in the future.

However, the take-home message from this trial remains that treatment of asymptomatic GOR with lansoprazole in children with mild-to-moderate poorly controlled asthma was not beneficial; it may in fact cause an increase in respiratory infections. Further trials should be performed in patients with severe asthma, where therapy is either limited or toxic and should concentrate on identifying which subgroup of patients may benefit from anti-reflux therapy.

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