Symptomatic Viral Infection Is Associated With Impaired Response to Treatment in Children With Acute Asthma


PURPOSE OF THE STUDY. To examine the influence of viral respiratory infection (VRI) on treatment response in acute asthma.

STUDY POPULATION. A total of 218 children (mean age, 6.6 years) with acute asthma were recruited.

METHODS. Clinical symptoms were recorded, an asthma severity score was determined, and, whenever possible, a per-nasal aspirate was obtained for detection of viruses. Each child’s response to inhaled β₂-agonists was assessed after 6, 12, and 24 hours.

RESULTS. The 168 children with VRI symptoms received more treatment with inhaled β₂-agonists after 6 hours (P = .01), 12 hours (P = .002), and 24 hours (P = .0005) compared with the 50 children without such symptoms. Asthma severity did not differ between the 2 groups. A per-nasal aspirate was obtained from 77% of the children. The most frequently identified virus was rhinovirus (61.4%). Among children with symptoms of a VRI, those with rhinovirus had an impaired response to β₂-agonists at 6 hours (P = .032).

CONCLUSIONS. Children with acute asthma and symptoms of VRI respond less effectively to β₂-agonists after 6, 12, or 24 hours and thus may benefit from more intense therapy and monitoring.

REVIEWER COMMENTS. An association between viral upper respiratory infections and exacerbations of asthma has been recognized for many years and, specifically, rhinovirus appears to have a unique and stronger relationship with acute asthma in children compared with other viruses. The authors state that the identification of VRI symptoms at the initial assessment would be of potential clinical importance because children presenting clinically with such symptoms may benefit from more intensive therapy and monitoring. Potential limitations to this study included (1) the investigators were unable to obtain a per-nasal aspirate for virus detection in all study subjects; (2) as opposed to the administration of β₂-agonists as the primary measure of clinical response, more objective measures, such as spirometry or use of oral corticosteroids, may have been better measures to assess; and (3) the timing of other treatment administered before presentation to the emergency department, duration of the preceding infection, and/or allergen exposure was not completely controlled for in this study. Despite these issues, this study presents interesting clinical findings.

Interruption or Daily Montelukast Versus Placebo for Episodic Asthma in Children


PURPOSE OF THE STUDY. To investigate the efficacy of montelukast in the treatment of young pediatric patients with episodic asthma.

STUDY POPULATION. Children aged 6 months to 5 years with a history of asthma symptoms during the past year and symptom-free periods between episodes were included in this multicenter (111 sites), randomized, double-blind, double-dummy trial that took place from November 2006 to August 2009.

METHODS. Patients were randomized to 1 of 3 groups: daily montelukast plus intermittent, episode-driven placebo; daily placebo with montelukast given during episodes; or daily placebo with placebo given during episodes. Doses were given at night. Episode-driven medications were given for 12 days from the start of the episode. All patients could use short-acting β₂-agonists as needed for symptom relief. Action plans were given to the families. On a daily basis, symptom calendars were completed by parents, which included respiratory symptoms and use of medication for the treatment. During episodes of asthma, questions included day and night symptoms, use of asthma medications, limitation of activity, and use of health care resources. The primary endpoint was the number of episodes leading to an asthma attack that led to utilization of health care...
RESULTS. Almost 600 patients were randomized to each treatment arm. Almost 75% of patients had a least 1 episode of asthma, with almost half of patients culminating in an exacerbation. No significant difference was seen between groups in the number of episodes leading to asthma exacerbations. Daily montelukast reduced symptoms over the 12-day treatment period of asthma episodes compared with placebo ($P = .045$). β-Agonist use was reduced with both daily ($P = .048$) and intermittent ($P = .028$) montelukast compared with placebo. However, because of prespecified rules for multiplicity adjustments (requiring a positive primary endpoint), statistical significance for secondary endpoints could not be concluded.

CONCLUSIONS. The number of asthma episodes leading to asthma exacerbations over a yearlong period in these young pediatric patients was not reduced by montelukast use, although improvements occurred in some endpoints.

REVIEWER COMMENTS. The treatment of pediatric patients with severe intermittent asthma is challenging for clinicians. The optimal treatment for these patients is unknown; studies do not show benefits of preventive medications as in other forms of persistent asthma. This study did not show improvement in the number of asthma exacerbations requiring utilization of health care resources with the use of montelukast, although some secondary endpoints were suggestive. The need exists for further studies to improve the prevention of the morbidity seen during the asthma exacerbations of these patients.

Lansoprazole for Children With Poorly Controlled Asthma: A Randomized Controlled Trial

PURPOSE OF THE STUDY. To study the efficacy of proton pump inhibitor (PPI) therapy over 24 weeks in reducing symptoms in asthmatic children without symptomatic gastroesophageal reflux (GER) who had poor asthma control.

STUDY POPULATION. Subjects were between 6 and 17 years old with physician-diagnosed asthma and “labile airways function” defined as (1) 12% or greater increase in postbronchodilator forced expiratory volume in 1 second (FEV1), (2) methacholine PC20 less than 16 mg/mL, or (3) positive exercise challenge with a 20% or greater decrease in FEV1.

METHODS. This is a multicenter, randomized, double-masked, placebo-controlled parallel clinical trial in children with asthma. All subjects were on stable doses of inhaled corticosteroids and had poor asthma control defined by study specific criteria. Subjects were excluded if they self-reported any symptoms of GER requiring treatment with a PPI or other reflux medication. The primary outcome was change in asthma control questionnaire score at the 24-week visit. Secondary outcomes included rate of acute episodes of poor asthma control, change in Asthma Symptom Utility Index, change in Asthma Control Test, change in asthma-specific quality of life for children score, methacholine PC20, spirometry, FeNO, gastrointestinal symptoms, and nocturnal awakenings. Esophageal pH studies were performed before randomization in a subset. Participating children were randomly assigned to receive lansoprazole dosed by weight.

RESULTS. One hundred forty-nine children were randomized to lansoprazole therapy and 157 were randomized to placebo. Mean age at randomization was 11 years in both groups. More than 88% of participants completed the study. Of 115, 49 (43%) 24-hour pH probe studies demonstrated abnormal esophageal acid exposure. Gastrointestinal symptom scores were not different between patients with normal versus abnormal pH studies. No differences were seen in initial prebronchodilator FEV1 or forced vital capacity in those with normal or abnormal pH studies. At week 24 of therapy, mean Asthma Control Questionnaire score had decreased by $<.05$ (the predetermined clinically important difference) in both groups and was not statistically different between the 2 groups ($P = .12$). There were no statistically significant treatment effects for any of the secondary outcome measurements. In a subanalysis of the children with abnormal pH probe studies ($n = 49$), there was no significant effect of lansoprazole treatment for 24 weeks on any of the study outcomes. Adverse event monitoring showed treatment with lansoprazole was associated with statistically greater prevalence of upper respiratory tract infection, sore throat, and bronchitis. Activity-related bone fractures were seen in 6 of 149 lansoprazole-treated subjects and 1 of 157 placebo-treated children ($P = .06$).

CONCLUSIONS. In children 6 to 17 years old with mild or moderate persistent asthma on inhaled corticosteroids, without GER symptoms, abnormal pH probe diagnostic of GER disease is present in 43%. Yet 24-week treatment with lansoprazole had no significant effect on measures of asthma control, quality of life, lung function, or bronchial responsiveness compared with placebo in the total group and in the subgroup of patients with abnormal pH probe studies. Increased adverse events, upper
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