parents and physicians and may affect compliance with treatment. There was no adverse effect at this particular dose range, but we cannot assume this can be extrapolated to higher doses or other formulations. This study would be strengthened if the authors also showed the oral steroid exposure rate for each group, as increased oral steroid use among the placebo group compared with the treatment group could potentially lead to a result of no difference when one might exist. It should be noted that 2 of the authors previously worked for the company that manufactures the medicine and supported the study.


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Genomewide Association Between GLCCI1 and Response to Glucocorticoid Therapy in Asthma

PURPOSE. To determine the genetic basis for the individual variability response to inhaled glucocorticoid (ICS) therapy.

STUDY POPULATION. The primary study population was the Childhood Asthma Management Program cohort of 1041 children with asthma who were 5 to 12 years old at enrollment. Additional subjects were selected from 3 other National Institutes of Health–sponsored clinical trials.

METHODS. The study analyzed a small number of statistically powerful variants selected on the basis of a family-based screening algorithm. Single-nucleotide polymorphisms predicted the changes in lung function response to ICS.

RESULTS. Significant pharmacogenetic association was found in the single-nucleotide polymorphism, rs37972, replicated in 4 independent populations totaling 935 persons (P = .0007), which maps to the glucocorticoid-induced transcript 1 gene (GLCCI1) and is in complete linkage disequilibrium (ie, perfectly correlated) with rs37973. Both rs37972 and rs37973 are associated with decrements in GLCCI1 expression. Overall, the mean increase in forced expiratory volume in 1 second in the treated subjects who were homozygous for the mutant rs37973 allele was only about one-third of that seen in similarly treated subjects who were homozygous for the wild-type allele (3.2% ± 1.6% vs 9.4% ± 1.1%). The risk of poor response was significantly higher (odds ratio 2.36; 95% confidence interval 1.27–4.41) with genotype, accounting for 6.6% of overall ICS response variability.

CONCLUSIONS. The functional GLCCI1 variant is associated with substantial decrements in response to ICS in patients with asthma.

Age and Risks of FDA-Approved Long-Acting β2-adrenergic Receptor Agonists

PURPOSE OF THE STUDY. This meta-analysis investigated the relationship between adverse asthma-related events and long-acting β2-adrenergic receptor antagonists (LABAs) among different age groups. Previous studies have suggested a correlation between increased risk and LABA use that seems most pronounced among children.

STUDY POPULATION. The meta-analysis included 110 trials with 60,954 patients, 9807 of whom were children between the ages of 4 and 18 years. All trials included were randomized controlled trials of LABAs for the treatment of asthma. Only Food and Drug Administration (FDA)-approved LABA products and doses were included.

METHODS. The FDA-identified controlled trials comparing the risks of LABA to no LABA use in subjects by age group: 4 to 11, 12 to 17, 18 to 64, and >64 years. The primary composite end point was asthma-related death, intubation, or hospitalization. Subgroup analysis included patients with use of any amount of concomitant inhaled corticosteroid (ICS) and those assigned to regular ICS use.

RESULTS. The composite event incidence difference for the LABA group compared with the non-LABA group was 6.3 events per 1000 patient-years (95% confidence interval: 2.2–10.3). A correlation was observed between decreasing age and increasing incidence difference (P = .020), with the greatest incidence difference occurring in the youngest age group of 4 to 11 years (30.4 events per 1000 patient-years [95% confidence interval: 5.7–55.1]). The overall incidence difference and age trend were similar in the subgroup using any amount of concomitant ICS; however, among those assigned regular ICS use, there was neither an age trend nor a statistically significant increase in events with LABA use, except in patients >64 years.

CONCLUSIONS. The results of this meta-analysis suggest a higher incidence of asthma events associated with LABA use and show a trend between decreasing age and increased LABA risk; however, this increased risk among LABA users was not observed in a subgroup also prescribed...
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.
Age and Risks of FDA-Approved Long-Acting β₂-adrenergic Receptor Agonists

David R. Scott and Susan Laubach

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