the first few hours of an acute asthma exacerbation and that their effect occurs within the first 6 to 8 hours after administration. Inhaled corticosteroids have been suggested to work faster than oral or parenteral corticosteroids in the emergency setting. This study was undertaken to investigate the mechanism through which inhaled steroids may act faster than oral steroids for acute asthma.

STUDY POPULATION. The study included patients aged 16 to 65 years who were treated in the emergency department for moderate asthma exacerbations. Inclusion criteria included a previous diagnosis of asthma and no use of intravenous or oral steroid in the 4 weeks preceding the study.

METHODS. This study was a randomized, double-blind, placebo-controlled prospective trial. There were 39 patients aged 16 to 65 years assigned to receive fluticasone and placebo prednisone (19 patients) or prednisone and placebo fluticasone (20 patients). The medication was administered via a metered-dose inhaler and spacer (16 puffs, 4000 μg/day or placebo) plus 1 pill (prednisone 30 mg/day or placebo). Spirometry and induced sputum for differential cell counts and albumin, α1-macroglobulin and blood eosinophil, interleukin 5, and granulocyte-macrophage colony-stimulating factor levels were obtained before treatment and 2, 4, 6, and 24 hours after treatment.

RESULTS. Clinical symptoms (moderate-to-severe dyspnea) improved after 24 hours in both groups. Airway obstruction was similar between groups at baseline in peak expiratory flow and forced expiratory flow in 1 second, improving progressively during the first 6 hours and decaying slightly after 24 hours. There were no significant differences between treatment groups. Eosinophil counts in sputum also improved over time in both groups. The effect was faster with fluticasone than with prednisone but was partially lost at 24 hours. In contrast, prednisone reduced blood eosinophil counts, whereas fluticasone reduced airway eosinophils, suggesting a less systemic antiinflammatory effect of inhaled fluticasone.

CONCLUSIONS. Both treatments resulted in improved symptoms, airway obstruction and inflammation, and plasma protein leakage at 24 hours. Prednisone seemed to have reduced blood eosinophil counts, whereas fluticasone reduced airway eosinophils, suggesting a less systemic antiinflammatory effect of inhaled fluticasone.

REVIEWER COMMENTS. The role of inhaled steroids during an acute asthma exacerbation is unclear. There is insufficient evidence that inhaled steroids alone are as effective as systemic corticosteroids for treatment of acute asthma. The authors showed that there was no significant difference between high-dose fluticasone and oral prednisone in reducing airway obstruction and treatment of symptoms. This is particularly interesting, because inhaled steroids are less systemically active as compared with either intravenous or oral steroids and may confer fewer adverse effects. Of note, however, is the tremendously high dose of fluticasone used in the study. All study subjects had a 3-week follow-up visit, yet the authors failed to mention any relapses or continued morbidity of the subjects’ asthma symptoms. It would be of great importance to observe whether patients treated only with inhaled steroids are able to regain control of their asthma symptoms in the same manner as those patients treated with systemic steroids. Moreover, further investigations are warranted to elucidate whether lower doses of fluticasone can produce similar effects on symptoms of asthma exacerbations and airway obstruction.

β2 Adrenoceptor Polymorphisms Predict Response to β2-Agonists in Children With Acute Asthma


PURPOSE OF THE STUDY. To evaluate the influence of single-nucleotide polymorphisms in the β2-adrenoceptor gene on the response to inhaled β2 agonists in children with acute asthma exacerbations.

STUDY POPULATION. There were 148 children aged 2 to 16 years presenting to the emergency department (ED) with an acute asthma exacerbation recruited between July 2002 and September 2004.

METHODS. The ED physician’s diagnosis was based on the presence of wheezing with increased difficulty of breathing. Children were excluded if they had wheeze attributable to other factors (ie, cystic fibrosis, bronchopulmonary dysplasia, foreign body). The standard management of children presenting with an asthma exacerbation included oxygen if saturations were ≤94%, β2 agonist (salbutamol) and an anticholinergic (ipratropium bromide) via metered-dose inhaler with large-volume spacer at 20-minute intervals for the first hour, and prednisolone 1 mg/kg (maximum 40 mg). The initial severity of the asthma episode was determined by using a previously validated scoring system with a possible score of 5 to 15 (5–7 indicated mild; 8–11, moderate;
Effect of ADRB2 Polymorphisms on Response to Longacting β2-Agonist Therapy: A Pharmacogenetic Analysis of Two Randomised Studies


PURPOSE OF THE STUDY. To determine if polymorphisms at amino acid 16 of the β2-adrenergic receptor (ADRB2) affect response to long-acting β2-agonists in combination with inhaled corticosteroids (ICSs).

STUDY POPULATION. The study included individuals at least 12 years old (2225 in study 1 and 405 in study 2) who had asthma for at least 6 months and used ICSs.

METHODS. In study 1, individuals with at least 12% reversibility of their forced expiratory volume in 1 second received 6 months of double-blind treatment with budesonide plus formoterol for maintenance and reliever therapy, fixed-dose budesonide plus formoterol, or fixed-dose fluticasone plus salmeterol. The primary outcome was the time to first severe asthma exacerbation. In study 2, participants received 7 months of open-label treatment with an adjustable regimen of budesonide plus formoterol, fixed-dose budesonide plus formoterol, or fixed-dose fluticasone plus salmeterol. Primary outcomes included the number of asthma exacerbations, time to first exacerbation, and percentage of participants with at least 1 exacerbation. Participants were stratified according to ADRB2 genotype, and the relation between genotype and asthma outcome was determined.

RESULTS. Baseline characteristics were similar among all Gly16Arg genotypes, and the genotypes were equally distributed across treatment groups. A combination of the 3 treatment groups showed a similar likelihood of having >1 severe asthma exacerbation for each genotype in study 1 (Gly/Gly, 12%; Gly/Arg, 11%; and Arg/Arg, 9%) and study 2 (Gly/Gly, 9%; Gly/Arg, 8%; and Arg/Arg, 9%). The time to first exacerbation was similar among genotype groups (study 1 P = .31, study 2 P = .94). In study 1, there was no interaction among treatment group, genotype, and time to first severe exacerbation (P = .88). Improvement of morning peak expiratory flow and other secondary end points was similar for all genotypes in both studies. In study 2, differences in response according to genotype were not seen between participants with and without baseline reversibility of forced expiratory volume in 1 second.

CONCLUSIONS. Individuals with asthma may continue to receive ICSs plus long-acting bronchodilators regardless of their Gly16Arg genotype.

REVIEWER COMMENTS. Study results have varied regarding the effectiveness of long-acting β2-agonists, with or without...
$\beta_2$ Adrenoceptor Polymorphisms Predict Response to $\beta_2$-Agonists in Children With Acute Asthma

David Jeong and Harvey L. Leo

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