apy in a managed care setting received preventive therapy or prescribed medications for osteoporosis and to identify patient and provider characteristics associated with treatment.

Study Population and Methods. A cohort of 224 health plan enrollees 20 years and older who were dispensed at least 1 oral glucocorticoid prescription per quarter during the period October 1997 through September 1998 was identified from administrative data. Medical charts and administrative data were reviewed to determine use of preventive therapy and prescribed medications for osteoporosis.

Results. Of the 224 patients, 62% had at least 1 documented intervention aimed at osteoporosis prevention (counseling about calcium or vitamin D or weight-bearing exercise; prescription for estrogen, calcitonin, or bisphosphonate; or a bone mineral density study). Women were more likely than men to receive intervention (76% vs 44%; prevalence odds ratio: 4.41; 95% confidence interval: 2.17–9.10). Patients receiving a mean daily prednisone dose of 10 mg or more or 5 to <10 mg were no more likely to receive intervention than those receiving 5 mg or less prednisone daily. Sixty-two (90%) of 69 patients who were prescribed glucocorticoid therapy by rheumatologists had at least 1 intervention documented compared with 29 (48%) of 60 for internists, 26 (55%) of 47 for pulmonologists, and 22 (46%) of 48 for all other physicians. In a multiple logistic regression model, including patient age, sex, mean daily glucocorticoid dose, and physician specialty, women and patients prescribed glucocorticoids by a rheumatologist were significantly more likely to receive intervention aimed at osteoporosis prevention.

Conclusions. A substantial proportion of patients receiving long-term glucocorticoid therapy do not receive preventive therapy for osteoporosis. Efforts should be made to reduce barriers to such treatment and increase the proportion of patients given preventive therapy.

Reviewer’s Comments. This issue remains important. Over half the patients in this study had either asthma or chronic obstructive pulmonary disease. Nonetheless, I’m just not treating very many asthmatic patients with oral corticosteroids these days, so it just doesn’t come up very often. As I understand it, it’s been difficult demonstrating that inhaled corticosteroids cause osteopenia.

ALLEN ADINOFF, MD
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LEUKOTRIENE ANTAGONIST THERAPY

EFFECTS OF ZAFIRLUKAST UPON CLINICAL, PHYSIOLOGIC, AND INFLAMMATORY RESPONSES TO NATURAL CAT ALLERGEN EXPOSURE


Purpose of the Study. Leukotriene receptor antagonists have been shown to attenuate physiologic changes in the upper and lower airways induced by inhaled allergen challenge. This study looks at the effects of the oral leukotriene receptor antagonist zafirlukast on natural exposure to cat in patients with cat allergy. This study examines clinical, physiologic and inflammatory responses of the upper and lower airways.

Study Population. Eighteen asthmatic patients between the age of 12 and 65 participated. All patients had a positive prick skin test to cat allergen and a positive response to a screening cat room challenge. At the time of study entry, all subjects were free of upper and lower respiratory tract symptoms.

Methods. This study used a randomized, double-blind, placebo-controlled cross-over design. Two weeks after the screening cat challenge, the patients were randomized to receive either zafirlukast 20 mg bid or placebo for 7 days before the first cat room challenge. All other allergic and asthmatic medications were held per standard protocol. Then, after a 14-day washout period, the patients were crossed-over to receive the alternate therapy for a week and then receive a second cat room challenge. Clinical symptoms, pulmonary function and sputum and nasal lavage fluid, cell and eosinophil cationic protein (ECP) measurements were performed before and after each natural cat challenge.

Results. Fel d 1 concentrations were measured and were similar during both the placebo and the zafirlukast challenges. After cat challenge, zafirlukast significantly reduced scores for both wheezing (P = .0004) and chest tightness (P = .019) compared with placebo. Symptom scores for the upper airways (congestion, rhinorrhea, itching, sneezing) did not meet statistical significance between the 2 treatments. After 7 days of treatment, prechallenge FEV1 was significantly higher with zafirlukast vs. placebo (P = .001). After cat exposure, zafirlukast significantly attenuated the decrease in forced expiratory volume in 1 second (FEV1) compared with the placebo (−15.1% vs −25.1%; P = .019). The occurrence of late asthmatic responses during the study was low, with 1 placebo-treated patient and 3 zafirlukast-treated patients demonstrating changes in pulmonary function between 2 and 12 hours after cat challenge. Analysis of induced sputum demonstrated no statistically significant differences between zafirlukast and placebo in total cell counts, cell differential, or ECP before or after challenges. Analysis of nasal lavage fluid revealed significantly fewer total cells and absolute counts of lymphocytes, neutrophils, monocytes, and basophils for zafirlukast compared with placebo after challenge, but there were no statistically significant differences in absolute or percentage eosinophils or ECP.

Conclusions. Zafirlukast 20 mg bid for 1 week demonstrated a significant protective effect on symptoms of asthma and alterations in pulmonary function induced by natural cat exposure. There were no effects noted on nasal symptoms, and no difference in the number of eosinophils or ECP in the upper or lower airway was seen with active treatment versus placebo.

Reviewer’s Comments. A similar trial (J Allergy Clin Immunol. 2000;105:704–710) also demonstrated a significant improvement in FEV1 postchallenge at 15 and 30 minutes but not at 45 and 60 minutes. This study also showed improvement in both lower and upper respiratory symptoms and intranasal anatomy measured by acoustic rhinometry. Other studies have also shown that leukotriene receptor antagonists in Food and Drug Administration (FDA)-approved doses do not affect airway eosinophilia after a single allergen exposure. Only 1 study has been published to date looking at long-term use of montelukast in asthma showing attenuated sputum eosinophilia with chronic therapy.

ALAN B. GOLDSOBEL, MD
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A COMPARISON OF SHORT-TERM TREATMENT WITH INHALED FLUTICASONE PROPIONATE AND ZAFIRLUKAST FOR PATIENTS WITH PERSISTENT ASTHMA

Purpose of the Study. To compare the short-term efficacy and safety of low-dose fluticasone propionate with that of oral zafirlukast therapy for patients previously treated with β₂-agonists alone, and to evaluate the potential therapeutic benefit of switching from zafirlukast to a low-dose inhaled corticosteroid.

Subjects and Methods. This study consisted of a 4-week randomized, double-blind treatment period followed by a 4-week open-label period. Two hundred ninety-four patients ≥12 years old with asthma previously uncontrolled with β₂-agonists alone were randomly assigned to treatment with low-dose inhaled fluticasone (88 µg twice daily) or oral zafirlukast (20 mg twice daily). After 4 weeks, all patients discontinued their double-blind therapy and received open-label fluticasone (88 µg twice daily). Outcomes included pulmonary function, asthma symptoms, albuterol use, asthma exacerbations, and adverse events.

Results. During the double-blind treatment period, fluticasone patients had significantly greater improvements in morning peak flow (29.3 L/min vs 18.3 L/min), percentage of symptom-free days (19.8% vs 11.6%), and daily albuterol use (−1.8 puffs per day vs −1.1 puffs per day) compared with zafirlukast patients (P < .025, each comparison). During the open-label period, patients switched from zafirlukast to fluticasone experienced additional improvements in morning peak flow (17.2 L/min), evening peak flow (13.6 L/min), and forced expiratory volume in 1 second (FEV₁) (0.11 liter) and daily albuterol use (−0.9 puffs daily) compared with values obtained at the end of the double-blind treatment period (P < .001, each comparison).

Conclusions. Low-dose fluticasone was more effective than zafirlukast in improving pulmonary function and symptoms in patients with persistent asthma. In addition, switching patients from zafirlukast to fluticasone further improved clinical outcomes.

Reviewers’ Comments. The emerging consensus is that inhaled corticosteroids, in general, are more effective monotherapy for asthma than are leukotriene receptor antagonists, at least in short-term studies. Certainly, however, many individual patients with mild persistent asthma will do very well taking only leukotriene receptor antagonists. In addition, long-term studies may suggest at least similar benefits due to improved compliance with oral medications.

Allen Adinoff, MD
Aurora, CO

MONTELUKAST ADDED TO Budesonide in Children with Persistent Asthma: A Randomized, Double-Blind, Crossover Study


Purpose of the Study. The possible additive effects of leukotriene antagonists and inhaled corticosteroids have not been studied in children. This study sought to determine whether the addition of montelukast to budesonide would improve asthma control in children with inhaled glucocorticoid-dependent persistent asthma.

Study Population. A total of 279 children with asthma with persistent asthma on inhaled corticosteroid therapy.

Methods. This was a multicenter, randomized, double-blind, crossover study. After a 1-month run-in on budesonide 200 µg twice daily, children were randomized to receive montelukast 5 mg daily or placebo over the next 4 weeks, after which they were crossed-over to the opposite treatment for the next 4 weeks.

Results. The mean age was 10.4 ± 2.2 years, the mean forced expiratory volume in 1 second (FEV₁) was 77.7% ± 10.6% predicted, and reversibility was 18.1% ± 12.9%. Compared with adding placebo to budesonide, adding montelukast produced significant improvements in the mean percent change from baseline FEV₁ (P = .062 [P = .010 for per-protocol analysis]), mean absolute change from baseline FEV₁ (P = .040), mean increase from baseline in morning (P = .023) and evening (P = .012) peak expiratory flows, decrease in exacerbation days by approximately 25% (P < .001), decreased β₂-agonist use (P = .013), and reduced blood eosinophil counts (P < .001). There were no significant differences with regard to safety.

Conclusion. The addition of montelukast to budesonide improved asthma control significantly, with improvements in lung function, symptoms, and the need for rescue medication.

Christopher Randolph, MD
Waterbury, CT

OTHER THERAPIES

THE ANTI-IGE ANTIBODY OMALIZUMAB REDUCES EXACERBATIONS AND STEROID REQUIREMENT IN ALLERGIC ASTHMATICS


Purpose of the Study. To demonstrate the clinical benefit and steroid-sparing effect of treatment with anti-immunoglobulin E (IgE) antibody, omalizumab, in patients with moderate-to-severe asthma.

Study Population. A total of 546 allergic asthmatics (aged 12–76 years), symptomatic despite inhaled corticosteroids (500–1200 µg daily of beclomethasone dipropionate) and demonstrating a positive skin prick test to dust mites, dog, or cat and a serum total IgE level of >30 and <700 international units (IU).

Methods. After a run-in period of 4 to 6 weeks, patients were randomized to receive either placebo or omalizumab subcutaneously every 2 to 4 weeks for 7 months. The interval was determined on dosing based on body weight and baseline IgE level. During the run-in period, patients were switched to inhaled beclomethasone using the dose at which they were stable. Dose was maintained during the first 16 weeks of the study. In the next 12 weeks, patients were seen every 2 weeks and inhaled steroid dose was decreased based on clinical symptoms and forced expiratory volume in 1 second (FEV₁). Lowest inhaled steroid dose was held for the remaining 4 weeks of the study. IgE levels were determined pre- and poststudy.

Results. There was a reduction in serum-free IgE from baseline by 89% to 99% for those patients on omalizumab. The number of asthma exacerbations per patient were statistically different in favor of omalizumab for both stable steroid and steroid reduction phases (P < .001). Percentage of patients with at least 1 asthma exacerbation was significantly lower in the omalizumab group (P < .001). During the steroid reduction phase, there were 52% fewer exacerbations in the omalizumab group versus the placebo group (P < .001) despite the greater reduction of the be-
A Comparison of Short-Term Treatment with Inhaled Fluticasone Propionate and Zafirlukast for Patients with Persistent Asthma

Allen Adinoff

*PEDIATRICS* 2002;110;463

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