**MEDICAL THERAPIES**

**Daily Versus As-Needed Corticosteroids for Mild Persistent Asthma**


**PURPOSE OF THE STUDY.** To determine the effectiveness of as-needed versus regular controller therapy in adults with mild persistent asthma.

**STUDY POPULATION.** A total of 225 adults with symptom criteria for mild persistent asthma and forced expiratory volume in 1 second (FEV₁) >70% predicted with >12% reversibility or PC₂₀ (provocative concentration causing a 20% decrease in FEV₁) methacholine at ≤16 mg/mL.

**METHODS.** Patients were assigned to 1 of 3 treatment groups: budesonide DPI 200 μg twice daily (BUD), oral zafirlukast 20 mg twice daily (ZAF), or placebo. The study was double-blind, double-dummy. At the beginning and the end of the study, all patients were treated with 0.5 mg/kg per day of prednisone, 800 μg twice a day of budesonide, and 20 mg twice a day of zafirlukast plus as-needed albuterol. Evaluation was accomplished by assessing asthma symptoms followed by pulmonary-function testing and gathering information on, albuterol use and exacerbations over the 1-year study.

**RESULTS.** For both of the primary efficacy outcomes, morning peak expiratory flow rate and exacerbations, there were no differences between the groups. Several outcomes were superior for the BUD group, including prebronchodilator FEV₁, bronchial reactivity, symptom scores, exhaled nitric oxide, asthma control score, and symptom-free days (26 more). Postbronchodilator FEV₁ and quality of life were not different between the groups. The as-needed group took budesonide, on average, for only one-half week during the study.

**CONCLUSIONS.** Adults with mild persistent asthma can be managed with high-dose budesonide on an intermittent basis. However, greater improvement in markers of airway inflammation and more symptom-free days (26 per year) occurred with regular use of low-dose budesonide.

**REVIEWER COMMENTS.** This is an adult study that focused on short-term outcomes, which may not translate to children. It is not known if similar results would be seen with a longer-term study.

**Safety of Budesonide Inhalation Suspension in Infants Aged Six to Twelve Months With Mild to Moderate Persistent Asthma or Recurrent Wheeze**


**PURPOSE OF THE STUDY.** To compare the safety of budesonide inhalation suspension (BIS) with placebo.

**STUDY POPULATION.** Infants (aged 6–12 months) with mild-to-moderate persistent asthma or recurrent wheeze.

**METHODS.** A multicenter, randomized, double-blinded, parallel-group, placebo-controlled study, in which 141 infants received 0.5 mg of BIS (n = 48), 1.0 mg of BIS (n = 44), or placebo (n = 49) once daily for 12 weeks. The primary variable was adrenal function, which was based on cosyntropin-stimulated plasma cortisol levels. Spontaneous adverse events and clinical laboratory findings were monitored.

**RESULTS.** Overall, the types and frequencies of adverse events reported during the study were comparable across treatment groups. The response to cosyntropin stimulation was similar across treatment groups, with no significant difference between BIS treatment and placebo.

**CONCLUSIONS.** The safety profile of BIS was similar to that of placebo, with no suppressive effect on adrenal function in patients 6 to 12 months of age with mild-to-moderate persistent asthma or recurrent wheeze.

**REVIEWER COMMENTS.** Inhaled corticosteroids remain the preferred choice for the long-term management of persistent asthma in pediatric patients. In addition, because BIS has become available for clinical use, more and more infants and young children with persistent asthma and/or recurrent episodes of wheezing have been managed with this inhaled antiinflammatory medication. In turn, appropriate questions have arisen from caregivers and providers about the overall safety of this therapy in these very young patients. Although the safety and efficacy of nebulized BIS have been confirmed in well-designed investigations in patients 6 months to 8 years of age, controlled clinical studies addressing the safety and efficacy of inhaled corticosteroids exclusively in the infant age range have been lacking. This current investigation provides very useful safety data for BIS in this understudied infant population. The data demonstrate that once-daily administration of BIS, 0.5 or 1.0 mg, was not associated with a decrease in adrenal function, which was based on cosyntropin-stimulated plasma cortisol levels. This information should be very useful to health care providers who prescribe this medication for
Long-term Safety of Once-Daily Budesonide in Patients With Early-Onset Mild Persistent Asthma: Results of the Inhaled Steroid Treatment as Regular Therapy in Early Asthma (START) Study


PURPOSE OF THE STUDY. Inhaled corticosteroids are the recommended treatment for all patients with persistent asthma. The aim of this study was to evaluate the safety and tolerability of long-term treatment of patients with mild persistent asthma with once-daily budesonide.

STUDY POPULATION. Seven thousand two hundred twenty-two patients (aged 5–66 years) with mild persistent asthma diagnosed within 2 years of study entry, with wheeze, cough, dyspnea, or chest tightness weekly and demonstration of reversible airway obstruction, were enrolled into the study.

METHODS. This was a prospective, double-blind, placebo-controlled study. Patients were divided into 2 groups according to age. Those patients younger than 11 years received 200 μg of budesonide via a dry-powder inhaler or placebo, and patients 11 years and older received 400 μg of budesonide via dry-powder inhaler or placebo. All treatments were administered for 3 years and in addition to the patients’ usual asthma therapy.

RESULTS. Overall, 21,520 adverse events were reported (10,850 in the budesonide group and 10,670 in the placebo group). The most commonly reported events were respiratory infections such as rhinitis, pharyngitis, bronchitis, viral infections, and sinusitis. Oral candidiasis was more common in the budesonide group (1.2%) than in the placebo group (0.5%); the frequencies of other adverse effects previously reported to be associated with inhaled corticosteroids (skin disorders, psychiatric disorders, and allergic reactions) were similar between the 2 groups. The number of deaths and serious adverse events were similar for children and adults in both treatment groups.

CONCLUSIONS. Three-year treatment with budesonide (200 or 400 μg) is safe and well tolerated in both children and adults who have recent onset of mild persistent asthma.

REVIEWER COMMENTS. This study shows not only that budesonide dramatically reduces the overall risk of experiencing a severe asthma-related event but also that budesonide has very little risk of causing any significant adverse events. One of the most difficult, yet very important tasks as a physician is to educate the patient that inhaled corticosteroids are not the enemy, but rather that the patient’s health is at greater risk from asthma itself. Clearly, early intervention is safe and effective. This study provides valuable information and should help patients and their families to feel comfortable with long-term inhaled corticosteroids use in asthma.

Budesonide/Formoterol Combination Therapy as Both Maintenance and Reliever Medication in Asthma


PURPOSE OF THE STUDY. Previous studies have shown that the combination of inhaled corticosteroids (ICSs) with long-acting β2 agonists improves asthma control and reduces exacerbations. The authors hypothesized that in patients already receiving daily budesonide/formoterol (B/F), replacing conventional short-acting β2 agonist (SABA) rescue with the B/F combination drug would increase antiinflammatory therapy while simultaneously giving rapid relief of symptoms. The investigators reasoned that using the B/F combination drug in this manner might reduce asthma exacerbations and improve asthma control compared with other possible regimens.

STUDY POPULATION. Subjects were 2760 patients with asthma (aged 4–80 years), all previously on ICSs.

METHODS. A double-blind parallel-group study was performed with subjects randomly assigned to 3 groups: B/F (80 mg/4.5 μg) twice daily for maintenance and also for rescue; B/F (80 mg/4.5 μg) twice daily with terbutaline 0.4 mg for rescue; or budesonide 320 μg twice daily with terbutaline 0.4 mg for rescue. Pediatric patients (11%–13% of each group) received half of the above-stated doses for maintenance. The primary outcome was time to first severe exacerbation, defined as asthma symptoms requiring an emergency department visit or hospitalization; an increase in ICS dose; use of oral steroids; or a morning peak expiratory flow rate ≤70% of baseline on 2 consecutive days.

RESULTS. Multiple positive outcomes were seen in the group using B/F for maintenance and rescue: a significant increase in the time to the first severe and mild exacerbations (P < .001); a 45% to 50% decrease in the number of severe exacerbations; significant decreases in the use of rescue medication, nighttime symptom score,
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