

ORIGINAL ARTICLE

Budesonide Inhalation Suspension Reduces the Need for Emergency Intervention in Pediatric Asthma: A Named-Patient Case Series

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ABSTRACT

This report describes 15 children aged 10–35 months frequently hospitalized with uncontrolled asthma who were monitored for a mean of 26.9 months to assess the efficacy of budesonide inhalation suspension (AstraZeneca LP, Wilmington, DE) in reducing emergency interventions. Budesonide inhalation suspension was previously shown to relieve asthma symptoms, improve pulmonary function, and reduce rescue medication use in children as young as 6 months with mild to severe persistent asthma. We now show that ≥ 1 year of treatment with budesonide inhalation suspension at doses between 0.25 and 1.5 mg/d decreased the burden of asthma. The mean number of hospitalizations caused by asthma or respiratory illness decreased from 1.8 ± 1.37 in the period before initiation of treatment with budesonide inhalation suspension to 0.33 ± 0.62 during treatment. Likewise, the mean number of oral prednisone courses decreased from 8.1 ± 13.7 to 1.8 ± 2.1 , and the mean number of acute respiratory illnesses requiring additional therapy decreased from 2.7 ± 2.3 before treatment with budesonide inhalation suspension to 0.87 ± 0.74 during treatment. Numbers of emergency department visits decreased or remained the same after initiation of budesonide inhalation suspension treatment in all but two children. There was no effect on growth rate in this group of children with moderate to severe asthma. In this case series, budesonide inhalation suspension represents a safe, effective treatment option to prevent recurrent emergency intervention for patients < 3 years of age with poorly controlled asthma.

Key Words: Asthma; Inhaled corticosteroid; Budesonide inhalation suspension; Nebulizer treatment; Pediatrics.

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INTRODUCTION

Asthma ranks as the leading serious chronic illness among children (1). Fifty percent to 80% of new asthma cases begin in children before age 5 (2), resulting in an estimated 1.3 million asthmatic children 5 years of age or younger in the United States (2). Asthma is a leading cause of hospitalization among children (3,4) and is associated with a high rate of emergency care. In 1999, there were nearly 658,000 pediatric emergency department visits due to asthma, with the highest annual rate (137.1 per 10,000) in the 0- to 5-year age group (1). Hospitalization is the greatest contributor to costs associated with asthma (5), and it has been suggested that reducing the number of pediatric asthma hospitalizations may offer the greatest potential for cost reduction (6).

Inhaled corticosteroids are the most effective anti-inflammatory agents for the treatment of asthma and are recommended in national and "best practice" guidelines for long-term asthma management (2,7,8). Astra-Zeneca LP, Wilmington, DE) is the only nebulized inhaled corticosteroid currently available. Although most inhaled corticosteroids are approved for children 6 years of age and older, budesonide inhalation suspension is approved in the United States for the treatment of asthma in children as young as 12 months and, thus, represents an important therapeutic option for infants and young children who are unable to use metered-dose or dry-powder inhalers. In three U.S., controlled clinical trials enrolling 1018 children 6 months to 8 years of age with mild to moderate persistent asthma, treatment with budesonide inhalation suspension significantly reduced asthma symptoms and improved pulmonary function compared with placebo (9–11). The results of European studies of budesonide inhalation suspension treatment in infants and children with severe asthma have shown reductions in asthma symptoms, use of rescue medication, and need for oral corticosteroids (12–14).

This report describes the effects of budesonide inhalation suspension on asthma-related health outcomes in young children with uncontrolled moderate to severe persistent asthma requiring repeated emergency intervention.

METHODS

Children 6 months to 8 years of age were enrolled between March 1997 and January 1999 as part of a named-patient program if they had severe, oral corticosteroid-dependent asthma not adequately controlled with other forms of therapy. Diagnosis of severe asthma was

based on National Heart, Lung, and Blood Institute criteria, which included daily use of systemic corticosteroids and short-acting β_2 -agonist for at least 3 months before enrollment and daily cough or wheeze. Children also must have had documented severe, dose-limiting side effects due to oral corticosteroid use and must have been unable to use or had disease that was refractory to other inhaled corticosteroids. Children were excluded from the program if they were intubated for an asthma exacerbation or hospitalized for respiratory failure within 90 days of enrollment. Children were treated with cromolyn sodium, ipratropium bromide, and as-needed short-acting β_2 -agonist before enrollment.

Budesonide inhalation suspension treatment was initiated to improve control of asthma, with starting doses and subsequent dose adjustments made at the discretion of the physician based on the clinical course of the disease. Children returned to the physician's office every 4–6 weeks for assessment. Asthma-related health outcomes, which were assessed before initiating treatment with budesonide inhalation suspension and at the end of the observed treatment period, included hospitalizations for asthma or respiratory tract infection, 1-week oral prednisone courses, emergency department visits, and the frequency of acute respiratory illness requiring additional therapy. Patient records, oral reports of serious adverse events, and patient histories were used to assess outcomes. Height, measured by stadiometry, and weight were obtained at office visits every 12 weeks. Effects on growth were assessed by summarizing the children's height and weight data, expressed as percentiles from the National Center For Health Statistics, at the start of treatment and at the end of the observation period.

Outcomes are presented as mean \pm standard deviations (SDs) for the periods before and during budesonide inhalation suspension treatment. In addition, yearly hospitalization rates, oral prednisone courses, and acute respiratory illnesses for the periods before and during treatment with budesonide inhalation suspension were calculated on an individual basis to adjust for differences in lengths of observation time before and after initiation of budesonide inhalation suspension. Yearly rates were calculated as the number of events divided by months of observation (before or during treatment) multiplied by 12.

RESULTS

This series of cases included 15 boys with a mean age at the start of observation of 20.6 months (range, 10–35 months). The children were evaluated for a mean



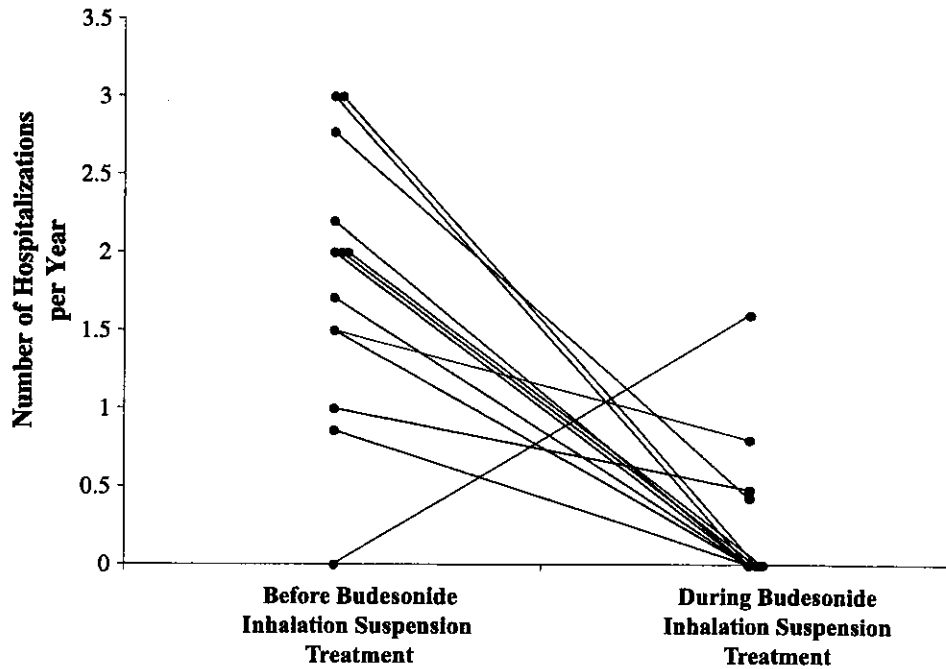


Figure 1. Numbers of hospitalizations for asthma and upper respiratory tract infection per year before and during budesonide inhalation suspension treatment in children with at least one recorded hospitalization.

of 12 months before receiving budesonide inhalation suspension and for a mean of 14 months while receiving budesonide inhalation suspension. The overall mean observation period was 26.9 months (range, 18–62 months).

Starting doses of budesonide inhalation suspension ranged from 0.25 to 1.5 mg/d, with a mean daily dose of 0.55 mg. Doses and dosing frequency varied considerably for many children throughout the treatment period. Compared with starting doses, doses at the end of

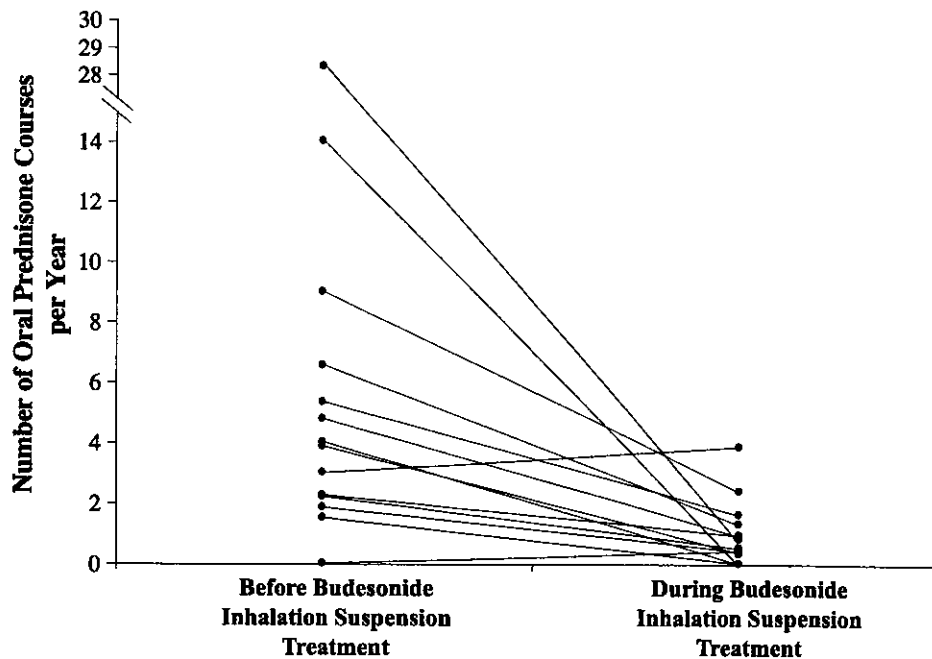


Figure 2. Numbers of 1-week oral prednisone courses administered per year to children before and during budesonide inhalation suspension treatment. Complete data were available for 14 children.

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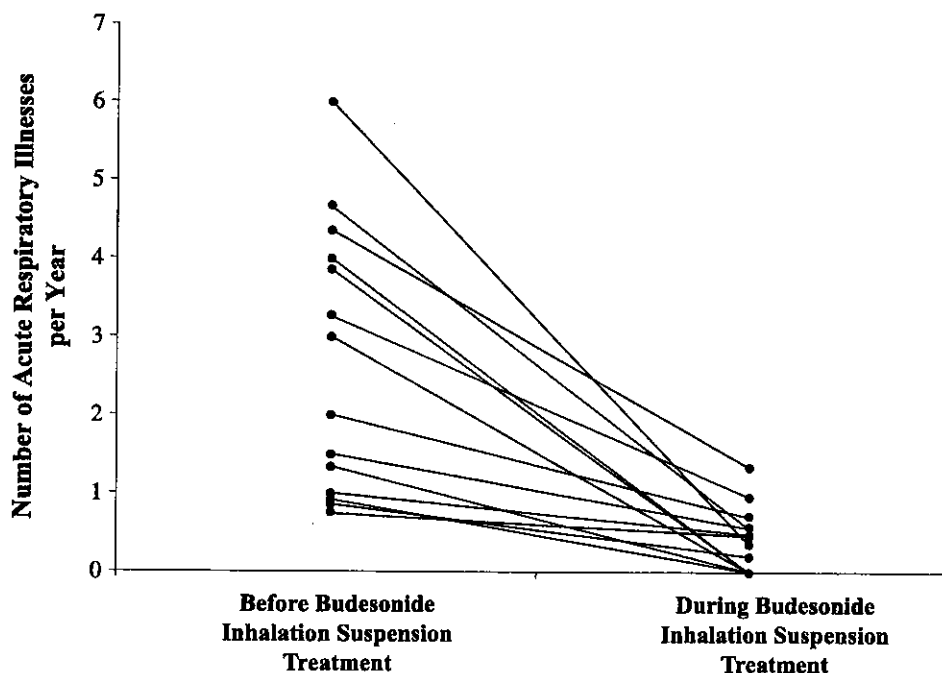


Figure 3. Numbers of acute respiratory illnesses per year in children before and during budesonide inhalation suspension treatment. Complete data were available for 14 children.

treatment increased in 10 children, decreased in 1 child, and remained the same in 4 children. The mean daily dose of budesonide inhalation suspension at the end of the observation period was 0.583 mg , with 12 of 15 children receiving once-daily dosing.

The mean number of hospitalizations due to asthma or respiratory tract infection decreased from 1.8 ± 1.37 during the period before treatment with budesonide inhalation suspension (mean 12-month observation period) to 0.33 ± 0.62 during treatment (mean 14-month observation). Only one child had an increased rate of hospitalization (from 0 to 1.6 hospitalizations per year) with budesonide inhalation suspension (Figure 1).

The mean number of 1-week oral prednisone courses decreased from 8.1 ± 13.7 to 1.8 ± 2.1 during the budesonide inhalation suspension treatment period, with yearly rates of use decreasing in all but two children receiving budesonide inhalation suspension (Figure 2). One child who had previously required daily prednisone treatment received only four prednisone bursts while receiving budesonide inhalation suspension. There was an average of 2.7 ± 2.3 episodes of acute respiratory illness requiring additional therapy before treatment with budesonide inhalation suspension, compared with a mean of 0.87 ± 0.74 episodes during treatment. The yearly rate of acute respiratory

illnesses decreased in all children after the initiation of budesonide inhalation suspension (Figure 3).

Two children had frequent (three each) emergency department visits before treatment with budesonide inhalation suspension. Of these two children, one had no emergency department visits recorded after the initiation of budesonide inhalation suspension treatment, and the other had only one emergency department visit recorded. Emergency department visits decreased or remained the same with budesonide inhalation suspension treatment in 11 of the remaining 13 children who had less frequent (≤ 1) emergency department visits before the initiation of budesonide inhalation suspension treatment; 10 children had no emergency department visits during treatment.

Treatment with budesonide inhalation suspension showed no adverse effect on growth. At the start of treatment, mean height and weight were in the 42.6 ± 30.2 and 52.3 ± 35.5 percentiles, respectively. At the end of the observed treatment period, mean height and weight increased so that patients were in the 48.1 ± 36.3 and 67.0 ± 29.0 percentiles, respectively.

DISCUSSION

budesonide inhalation suspension treatment significantly reduced morbidity in these 15 children with

uncontrolled asthma, as shown by the decreased numbers of hospitalizations for asthma and upper respiratory tract infections, of oral prednisone use, of acute respiratory illness, and of emergency department visits. Although conclusions from this descriptive case series report may be limited by the lack of a control group, the beneficial effects of budesonide inhalation suspension nonetheless support similar uncontrolled observations showing improved asthma control, decreased oral prednisone use, and reduced clinical admissions with budesonide inhalation suspension in 56 children (mean age, 35 months) with severe asthma despite maintenance therapy (14). Significantly reduced number of hospitalizations, urgent care visits, and oral prednisone use also have been shown in a long-term (4- to 6-year) controlled study of budesonide 200 µg twice daily administered by dry-powder inhaler in children 5–12 years of age with mild to moderate persistent asthma (15).

The patients presented in this series are of particular interest because patients with unstable asthma and those recently hospitalized for asthma often are excluded from clinical trials of asthma treatments. Also of note in this case series is the fact that the mean observation period (before and during treatment with budesonide inhalation suspension) was >2 years and that budesonide inhalation suspension doses were titrated at the discretion of the physician. Thus, this report provides important long-term, real-world information on a patient population that is underrepresented in controlled clinical trials of asthma treatments.

The results indicate that budesonide inhalation suspension can be titrated as needed to provide optimal asthma control at the lowest effective dose in these children with moderate to severe uncontrolled asthma, because asthma control improved considerably and few individuals showed any increase in emergency interventions during budesonide inhalation suspension treatment. Rates of oral corticosteroid courses increased in only two patients during treatment with budesonide inhalation suspension, and the hospitalization rate increased in only one. These differences may reflect observation periods during budesonide inhalation suspension treatment (15–30 months) that were considerably longer than observation periods before treatment (9–14 months).

The finding of no adverse effect on growth for budesonide inhalation suspension in the present report contrasts with findings of some previous studies showing early, transient reductions in growth velocity in children treated with inhaled budesonide (15,16).

Results of this case report series highlight the contribution of optimal therapeutic intervention with budesonide inhalation suspension in reducing emer-

gency interventions for pediatric asthma. Importantly, studies show that patient education and comprehensive case management also contribute to significantly reduce health resource use and costs due to asthma in children (17,18).

In summary, this case series presents important benefits of budesonide inhalation suspension treatment in a population of children with moderate to severe unstable asthma and supports the long-term use of nebulized budesonide inhalation suspension in the comprehensive management of pediatric asthma to prevent repeated emergency intervention and oral corticosteroid use.

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