double-blind, placebo-controlled, parallel-group study (Kemp JP, Skoner D, Szefler SJ, et al. Ann Allergy Asthma Immunol. 1999;83:231–239). This study retrospectively examines the data more closely and demonstrates that efficacy and safety are not dependent on whether administration is by facemask or mouthpiece. The results here provide reassuring data for clinicians treating children with persistent asthma who are too young to use mouthpieces. Similar results have also been reported for children in this age group with moderate persistent asthma (Mellon M, Lefelin J, Walton-Bowen K, et al. Am J Respir Crit Care Med. 2000;162:593–598).

Frank S. Virant, MD
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THE EFFECTIVENESS OF HIGH-DOSE INHALED BUDENOSIDE THERAPY IN THE TREATMENT OF ACUTE ASTHMA EXACERBATIONS IN CHILDREN


Purpose of the Study. The purpose of this study was to evaluate the efficacy of high-dose inhaled budesonide, in comparison to oral methylprednisolone, in the treatment of acute asthma exacerbations in children.

Study Population. Sixty children, ages 4 to 17 years, who had experienced an acute asthma exacerbation over a period of 6 months. All patients met the American Thoracic Society criteria for asthma.

Methods. Children who experienced an acute asthma attack unresponsive to home management, yet not severe enough to be hospitalized, were randomized into 2 groups. Group 1 received high-dose inhaled budesonide (1600 μg daily) plus dry powder terbutaline (2000 μg daily). Group 2 received oral methylprednisolone (1 mg/kg/day) plus inhaled budesonide (800 μg daily) plus dry powder terbutaline (2000 μg daily). Both groups were evaluated before treatment and 4 days after 3 complete days of treatment. Pre- and posttreatment pulmonary index scores, forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), FEV₁/FVC and forced expiratory flow 25%–75% (FEF25%–75%) were evaluated. Pulmonary index scoring (PIS) evaluated the physical examination findings of respiratory rate, severity of wheezing, inspiration/expiration ratio, and the use of accessory muscles.

Results. Thirty-one patients were in the high-dose budesonide group and 29 were in the methylprednisolone group. There were no significant differences in the demographics of the 2 groups, including such characteristics as age of disease onset, mean number of acute attacks in previous year and duration of symptoms at presentation. There were no significant differences between the 2 groups with respect to baseline PIS, FEV₁, FEV₁/FVC, or FEF25%–75%. A statistically significant decrease in PIS and a statistically significant increase in FEV₁, FEV₁/FVC, or FEF25%–75% were detected in both groups after 4 days of treatment. Comparison of the 2 groups revealed that the mean decrease in the PIS was 2.61 ± 1.12 in the group receiving high-dose budesonide and 1.90 ± 1.08 in the group receiving oral steroids (P = .038). No statistically significant differences were detected between the 2 groups with respect to the increase in lung function measurements (FEV₁, FEV₁/FVC, or FEF25%–75%). None of the patients who had received high-dose budesonide required treatment with oral steroids. During the follow-up period, 3 patients in the high-dose budesonide group and 8 patients in the oral steroids group needed to continue their therapy for 2 additional days because of incomplete recovery.

Conclusion. Short-term high-dose budesonide therapy can be considered as an alternative for children who are experiencing an acute asthma attack that is unresponsive to home management with regular use of inhaled β₂-agonist, yet who are not severe enough to hospitalize.

Reviewer’s Comments. This study supports an earlier study that demonstrated that high-dose budesonide was as effective as oral prednisolone over a 1 week period. An interesting finding in this shorter study is that with respect to clinical improvement, high-dose budesonide may be more effective than oral steroids plus medium-dose budesonide. Parents are extremely concerned about the use of steroids and the use of high-dose inhaled for mild exacerbations instead of oral steroids will most likely be well-received. This study is on the right track for future therapeutic options, although it should be noted that these patients only had mild exacerbations and that the results cannot necessarily be extrapolated to more severe episodes.

Helen Skolnick, MD
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BONE DENSITY IN ASTHMATIC CHILDREN TREATED WITH INHALED CORTICOSTEROIDS


Purpose of the Study. Inhaled corticosteroids (ICS) have been shown to have some systemic absorption and thus have some potential for adverse effects on bone density.

Study Population. A total of 20 prepubertal children (11 girls, 9 boys; aged 4–9 years, median age: 7.6 years) with chronic asthma taking moderate- to high-dose ICS for at least 12 months. The average doses used in μg/m²/day were beclomethasone 778 (n = 5), budesonide 819 (n = 9) and fluticasone 444 (n = 6).

Methods. Bone mineral density of vertebrae and distal radius measured by quantitative computed tomography. Bone mineral density values as well as heights were transformed into standard deviation scores and compared with normal values from healthy children.

Results. The values for bone mineral density, as well as for height, were not different than the expected values for normal children.

Conclusion. “ICS do not adversely affect bone mineral density in prepubertal asthmatic children.”

Reviewer’s Comments. We should still use as low a dose of ICS as possible, but this is yet another reassuring study that these very effective drugs are also very safe.

John M. Kelso, MD
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PERSISTENT WHEEZING IN INFANTS WITH AN ATOPIC TENDENCY RESPONDS TO INHALED FLUTICASONE


Purpose of the Study. To investigate the effect of inhaled fluticasone in a group of infants with significant wheezing at high risk of progressing to childhood asthma.

Study Population. A total of 52 infants between the ages of 3 to 12 months were recruited. Only 37 completed the study.

Methods. Study entry criteria also included a documented history of persistent wheeze, occurring at least 3
days/week for 6 weeks, persistent cough, occurring at least 3 nights/week for 6 weeks, or wheeze, occurring at least 3 times over the previous 3 months. Each child had either a personal history of eczema or a family history of allergy in a first degree relative. None of these children had been on inhaled corticosteroids. If oral steroids had been used, entry into the study was delayed 1 month after the steroid treatment. The study design was double-blinded, random-ized, and placebo-controlled. After a 2-week run-in period, the infants were randomized to receive either fluticasone propionate 150 μg as 3 puffs of 50 μg/puff twice a day using a spacer device or an identical placebo for 12 weeks. Albuterol by metered-dose inhaler was available for relief. Parents recorded symptoms of cough and wheeze twice a day. The symptoms were scored 0 to 3. Outcome measures were the mean daily symptom score and the number of symptom-free days. Pulmonary function testing was performed only at baseline. Serum immunoglobulin E (IgE) levels were also obtained during the run-in.

Results. Three groups were compared, those receiving fluticasone, those on placebo, and those who dropped out of the study. There were no differences between the groups in regard to number, sex, age, presenting symptoms, history of eczema, IgE level, family history of allergy, smoke exposure, or the presence of pets. In the fluticasone group, the average age was 9.8 months, 13/19 were males, 7/19 had eczema, 7/19 were exposed to parental smoke, and 9/19 had pet exposure. In the control group, the average age was 8.9 months, 14/18 were male, 9/18 had eczema, 7/18 were exposed to smoke, and 11/18 had pets. Only 27 infants underwent pulmonary function testing and there was no difference between the groups at baseline in their pulmonary function. There was a significant decrease in the fluticasone group in mean daily symptom scores at the end of the study compared with baseline and a significant difference when compared with the placebo group. At the end of the study, the symptom scores decreased 0.95/day with fluticasone while in the placebo group, the daily symptom score increased 0.17. There was also a significant increase in symptom-free days with fluticasone compared with baseline and compared with placebo. Growth parameters revealed a trend to slower weight gain and length in the fluticasone group. This was not found to be of statistical significance.

Conclusion. Symptom scores and symptom-free days were significantly improved with fluticasone in infants who had persistent disease and had a tendency towards allergy.

Reviewer’s Comments. This has all the problems of being a small and relatively short-term study, however, they did a very nice job at looking at a very specific population. This is a population of infants that can be most vexing to the pediatrician. What to do with the wheezing infant? What can be offered and in which infants will it work? Previous studies on the use of inhaled corticosteroids frequently included wide ranges of age and those who were without a predisposition to allergy. The clinical impact was variable leaving unanswered the question of the role of inhaled corticosteroids in young children. These infants were able to use a spacer device and a metered-dose inhaler. By the end of the study, there were 3.84 more symptom-free days over the previous 2 weeks as compared with the placebo group. Obviously more and longer studies of this sort are needed to help in the care of the wheezy infant.

FREDERICK E. LEICKLY, MD
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LOCAL SIDE-EFFECTS OF INHALED CORTICOSTEROIDS IN ASTHMATIC CHILDREN: INFLUENCE OF DRUG, DOSE, AGE, AND DEVICE


Purpose of the Study. To study the incidence of local side effects after inhaled corticosteroid use. There have been few studies in children documenting potential local effects. Identification and counseling for these potential effects may improve patient care and compliance.

Study Population. A total of 639 children with known asthma taking daily inhaled corticosteroid (budesonide or beclomethasone) therapy were divided into 2 groups, <6 and >6 years old.

Methods. Patients were prospectively enrolled in this cohort study. Clinical examination was performed and a questionnaire survey was completed by the patient and parent for symptoms during the previous month.

Results. Of the 639 children, the mean age was 75.9 ± 48.9 months (range: 3 months–16 years) and 61.3% were boys. In the beclomethasone (BDP) group, statistically significant variables included younger age, greater proportion of boys, lower steroid dose, and use of a pressurized metered-dose inhaler (pMDI). For both drugs the overall reported local side effects included at least 1 side effect in 61.5% of children, cough during inhalation in 39.7%, thirsty feeling in 21.9%, dysphonia in 14%, oral candidiasis in 10%, and perioral dermatitis in 2.9%. The incidence of cough during inhalation was doubled (53.7% vs 25.5%) when a spacer was used. Cough and perioral dermatitis were reported more frequently in children <6 years old while hoarseness was more common in older children. Incidence of oral candidiasis was unchanged regardless of the inhaler device or mouth-rinsing.

Reviewers’ Comments. The weakness of this study was recall bias during data collection and effects of confounding variables. Cough incidence either daily or with inhaler use was reported overall in 93% of patients. Although cough was concluded to be attributable to the spacer, this group also had a statistically significant younger patient age, male sex, and greater daily albuterol use suggesting other possibilities. Spacers clearly deliver inhaled medications more effectively to the small airways and should be a cornerstone of therapy. The lack of association between mouth-washing, inhaler device, and incidence of oral candidiasis is interesting. However, their criteria for candidiasis was frank thrush and this may have been underestimated. Recognition of potential local side effects and discussion with the family before medication initiation can promote better provider-patient relationships and hopefully improve medication compliance.

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Washington, DC

PREVENTION OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS: EXPERIENCE IN A MANAGED CARE SETTING


Purpose. Treatment with glucocorticoids is the leading cause of drug-induced osteoporosis. Currently available guidelines indicate that patients receiving long-term glucocorticoid therapy should receive measures to prevent osteoporosis. The purposes of this study were to examine whether patients receiving long-term glucocorticoid ther-
## Persistent Wheezing in Infants with an Atopic Tendency Responds to Inhaled Fluticasone

Frederick E. Leickly  
*Pediatrics* 2002;110:461

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