cantly greater proportion of ICS-treated patients were discharged early from the ED compared with those treated with either placebo or SCS (odds ratio: 4.7). Patients who received multiple ICS doses along with β agonists also had improvement in spirometric and clinical scores, with evidence of a dose-response relationship. There was a significantly lower admission rate in the patients treated with multiple-dose ICSs. The number of patients needed to treat with ICSs to prevent 1 hospital admission was 10.

CONCLUSIONS. This study suggests that ICS treatment provides early beneficial effects (1–2 hours) when they were used in multiple-dose amounts administered in time intervals of ≤ 30 minutes.

REVIEWER COMMENTS. This meta-analysis suggests that ICSs given early in multiple doses with β agonists may have a place in the ED for treatment of acute exacerbations of asthma. Previous studies have shown that asthmatic patients have a significant increase in airway mucosal blood flow compared with nonasthmatic patients. Repeated high doses of ICSs could work by decreasing airway blood flow, leading to enhanced bronchodilator action when administered simultaneously with β agonists. Additional study is needed to determine the most effective dose and delivery system in different patient populations to obtain an optimal effect.

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Secondary Prevention of Asthma by the Use of Inhaled Fluticasone Propionate in Wheezy Infants (IFWIN): Double-Blind, Randomised, Controlled Study


PURPOSE OF THE STUDY. To determine if the early use of inhaled fluticasone propionate in wheezy infants helps to prevent loss of lung function and progression of asthma later in childhood.

STUDY POPULATION. High-risk children (N = 1073) identified by having 1 atopic parent were followed prospectively until 2 wheezing episodes occurred or there was 1 wheezing episode longer than 1 month. Of these patients, 206 who met the inclusion criteria were randomly assigned: 104 to placebo and 102 to treatment. The median age was 1.2 years (range: 0.5–4.9 years). Eighty-six percent continued to be followed by their fifth birthday.

METHODS. Children were excluded if they had wheeze caused by bronchiolitis, were preterm (< 34 weeks' gestation), had other chronic lung disease or chronic illness, had previous inhaled corticosteroid (ICS) use, or were unable to use the inhaler. The treatment group was started on fluticasone propionate 100 μg twice daily. Randomly assigned patients were followed by monthly telephone calls for the first 3 months, if controlled, and then every 3 months until their fifth birthday. If symptoms were not under control by 3 months, then open-label fluticasone propionate 100 μg was added. Treatment was adjusted to the minimum necessary to control symptoms. Participants were allowed to use β agonists as needed. Parents were asked to keep daily diaries of symptom scores, reliever use, and unscheduled visits. At the age of 5, specific airway resistance (sRAW), forced expiratory volume in 1 second (FEV₁), airway reactivity, and postbronchodilator lung function were measured and compared.

RESULTS. There was no significant difference between those in the treatment group versus placebo in the proportion of children with current wheeze, physician-diagnosed asthma, use of asthma medication, or current wheeze, even when factoring the addition of those participants who added open-label medication. There was also no significant difference in FEV₁ (baseline or postbronchodilator), sRAW, or airway reactivity at 5 years of age in these groups. The 2 groups were similar in the number of children who required, and in the length of time to adding, open-label drug. Symptom scores, use of reliever medication, and unscheduled visits to the family doctor were similar until the third month, when children in the treatment group had lower median daily symptom scores, a trend toward less reliever medication, and significantly fewer visits than those in the placebo group. In the 2 open-label drug groups, there was a greater risk of current wheeze, current use of asthma medications, and current wheeze with asthma medications compared with those in the placebo group, although there was no difference in baseline or postbronchodilator FEV₁. However, there was a significantly higher sRAW in the treated groups, which represented decreased lung function.

CONCLUSIONS. The use of ICS in young children at risk for asthma with the earliest sign of recurrent wheezing had no significant effect on the natural history of wheezing, lung function, or airway reactivity by 5 years of age and only showed a small improvement on symptom scores and unscheduled physician visits after the third month of the study. Higher postbronchodilator sRAW showing reduced lung function was seen in children in the treated group compared with those in the placebo group.

REVIEWER COMMENTS. Evidence for the efficacy of ICS in infants and very young children remains unclear. It has been suggested that early use of ICS could be detrimental to the lung development on the basis of the sRAW scores of ICS-treated patients. However, children in both...
the treatment and placebo groups required the addition of fluticasone equally, which suggests that perhaps those in the treatment group had worse disease. Prestudy lung function was not tested, and individual atopic status was not assessed to determine if these 2 groups were truly equivalent. Studies are needed to determine if atopy is a confounding factor and whether controlling for allergen exposure in addition to ICS has an effect on asthma outcomes. This study and other similar studies suggest that ICS can improve asthma symptoms, but early use does not modify the disease.

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High-Dose Inhaled Fluticasone Does Not Replace Oral Prednisolone in Children With Mild to Moderate Acute Asthma

PURPOSE OF THE STUDY. To evaluate whether there is a significant difference in the degree of impairment in forced expiratory volume at 1 second (FEV1) in children with mild-to-moderate acute asthma treated with either inhaled fluticasone or oral prednisolone.

STUDY POPULATION. Sixty-nine children aged 5 to 17 years with a previous history of wheezing who presented to a tertiary care pediatric emergency department (ED) with acute asthma and an FEV1 between 50% and 79% predicted.

METHODS. This randomized, double-blind, double-dummy trial randomly assigned patients to receive either 2 mg of fluticasone via metered-dose inhaler (MDI) in the ED along with 500 µg of fluticasone via Diskus twice daily for 5 days (n = 35) or 2 mg/kg oral prednisolone in the ED along with 1 mg/kg prednisolone once daily for 5 days (n = 34). All children received scheduled, nebulized albuterol and ipratropium bromide in the ED and were given scheduled salmeterol and rescue albuterol on ED discharge. FEV1 was measured at baseline, 4 hours, and 48 hours.

RESULTS. At 4 hours, the patients in the prednisolone group had a significantly greater increase in FEV1 (29.8% ± 15.5%) compared with those in the fluticasone group (19.1% ± 12.7%; P = .001). By 48 hours, the difference in FEV1 between the groups was no longer statistically significant. In addition, the number of unscheduled asthma visits by 48 hours after ED discharge was significantly greater in the fluticasone group (4 of 32) than the prednisolone group (0 of 34).

CONCLUSIONS. Children with mild-to-moderate acute asthma improve faster on oral prednisolone than inhaled fluticasone.

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Assessment of Adrenal Suppression in Children With Asthma Treated With Inhaled Corticosteroids: Use of Dehydroepiandrosterone Sulfate as a Screening Test

PURPOSE OF THE STUDY. To evaluate dehydroepiandrosterone sulfate (DHEA-S), a corticotropin-dependent adrenal androgen precursor, as a possible marker for adrenal function and hypothalamic-pituitary-adrenal axis suppression in children treated with inhaled corticosteroids (ICs) compared with low-dose (0.5 µg/m² up to 1.0 µg) and standard-dose (250 µg) cosyntropin-stimulation testing.

STUDY POPULATION. Twenty-two patients with moderate-to-severe—persistent asthma receiving a medium-to-high dose of ICs for at least 6 months were enrolled (definition of median-to-high dose of ICs: budesonide >400 µg/day or fluticasone >176 µg/day for children <6 years old or >200 µg/day for those ≥6 years). Patients had received no more than 2 courses of systemic corticosteroid exposure of <10 days’ duration in the previous 6 months and no systemic corticosteroid in the 1 month before enrollment. The average age of the patients was 8.6 years (range: 2–12 years).

METHODS. After a 12-hour fast, morning cortisol, corticotropin, DHEA-S, and fasting blood sugar levels were measured. Cortisol was measured after the stimulation tests. A cortisol level of ≤18 µg/dL was considered abnormal (adrenal suppression).

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REVIEWER COMMENTS. Systemic corticosteroids are both historically and currently the mainstay treatment for acute asthma, given their ability to reduce hospitalizations, decrease relapses, regain asthma control, and improve lung function. However, the risks associated with the frequent use of oral corticosteroids have led researchers to search for an alternative treatment for acute asthma. Although previous studies have shown oral corticosteroids to be superior to inhaled steroids in severe acute asthma, the question remains as to whether inhaled corticosteroids could be used in mild and moderate asthma exacerbations. This study addressed this question and determined that oral corticosteroids are superior to inhaled steroids, even for mild exacerbations of asthma, in regard to relapse rate and time to FEV1 improvement. These findings support the current use of oral steroids for treatment of mild-to-moderate acute asthma.
Secondary Prevention of Asthma by the Use of Inhaled Fluticasone Propionate in Wheezy Infants (IFWIN): Double-Blind, Randomised, Controlled Study

Patricia Gomez Dinger and Michael S. Kaplan

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