**Study Population.** Five hundred eighteen patients, 5 to 12 years old with persistent asthma. Patients were receiving sodium cromoglicate, nedocromil sodium, and/or inhaled corticosteroids at stable doses for at least 1 month before entry in the study.

**Methods.** After the run-in period, all patients were randomized in a double-blind manner to receive 12 or 24 µg formoterol dry powder capsule or placebo capsule twice daily for 12 months. This was given in addition to their baseline antiinflammatory treatment, which was not changed. The primary study variable was the area under the curve for forced expiratory volume in 1 second (FEV₁) measured over 12 hours after the morning dose of study medication.

**Results.** The area under the curve for FEV₁ after the first treatment dose and after 3 and 12 months of treatment was significantly greater in patients receiving formoterol 12 µg and 24 µg than in patients receiving placebo (all P < .0062). Although numerically greater for formoterol 24 µg, there was no statistically significant difference in FEV₁ between the 2 active treatment doses. Compared with placebo, both doses of formoterol significantly improved am and pm peak expiratory flow rates. In the group treated with formoterol 24 µg twice daily, median symptom score and median dose of rescue medication at night were lower than during the run-in period, whereas with the 12-µg dose and the placebo group this did not change. Hospitalization for asthma was higher in the 2 formoterol groups than in the placebo group. The number of patients reporting asthma exacerbations during the study was the same for all 3 treatment groups.

**Conclusions.** In asthmatic children who are still symptomatic despite antiinflammatory therapy, the addition of formoterol 12 or 24 µg improves air flow obstruction, nocturnal symptoms, and the use of rescue medication. The regular use of long-acting β-agonists was safe and well-tolerated in this patient population.

**Reviewer's Comments.** Although the overall results are encouraging, the increase in hospitalization in the formoterol-treated patients is concerning. It is possible that this could result from a masking of airway inflammation with potent 12-hour bronchodilatation.

**BRONCHODILATOR THERAPY AND HYPERACTIVITY IN PRESCHOOL CHILDREN**


**Purpose of the Study.** Parents often report that nebulized albuterol makes their children “hyper.”

**Study Population.** Nineteen children with asthma 25 to 64 months of age whose parents thought that albuterol made their children overactive.

**Methods.** This was a double-blind, crossover study with children randomized to receive nebulization with albuterol (5 mg) or saline, then the reverse [Note: the usual dose is 0.5 mL of the 0.5% solution = 2.5 mg]. Behavior was rated by parents using Connors’ Rating Scale at baseline and after nebulization. Professional observers rated the level of activity using Preschool Behavior Observation Scale (PS-BOS).

**Results.** Parental ratings of activity revealed no significant difference between baseline and postalbuterol scores. Professional observers ratings of activity revealed no evidence of an increase in the child’s activity after administration of albuterol.

**Conclusions.** Neither parental report nor observer ratings suggested any significant increase in the child’s level of activity after albuterol.

**STEROID THERAPY**

**SIGNIFICANT VARIABILITY IN RESPONSE TO INHALED CORTICOSTEROIDS FOR PERSISTENT ASTHMA**


**Purpose of the Study.** Clinical studies have suggested that considerable variability exists among individuals with asthma in both their responsiveness to inhaled corticosteroids (ICS) and side effects from such drugs. A clinical model is needed to compare various ICS with respect to efficacy and safety, as no standardized model has yet been developed.

**Study Population.** Study subjects were corticosteroid-naïve individuals with mostly moderate persistent asthma who were 18 to 55 years of age. The study was designed as a feasibility study rather than a comparative trial.

**Methods.** Thirty subjects were randomized to receive either beclomethasone dipropionate (BDP) 168, 672, and 1344 µg/day (n = 15) or fluticasone propionate (FP) 88, 352, and 704 µg (n = 15) via metered-dose inhaler (MDI) with chlorofluorocarbon propellant and OptiChamber (Respironics, Cedar Grove, NJ) spacer in 3 consecutive 6-week intervals. Compliance was monitored with a Doser CT (Meditrack Products, Hudson, MA) device. All subjects then received 3 weeks of FP dry powder inhaler (DPI) 2000 µg/day. The primary outcome variable for assessing comparative efficacy was forced expiratory volume in 1 second (FEV₁). Secondary outcomes were methacholine PC-20, exercise-induced change in FEV₁, exhaled nitric oxide (eNO), and induced sputum eosinophilia. Overnight cortisol suppression was measured by collecting hourly blood samples from 7 pm to 7 am.

**Results.** Maximum FEV₁ response occurred with the lowest dose of FP and the medium dose of BDP and was not further increased by high-dose FP-DPI. Near-maximum improvement in methacholine PC-20 occurred with low-dose FP and medium-dose BDP. Responsiveness to ICS varied markedly among subjects. Good (>15%) FEV₁ response was associated with high eNO, high pretreatment bronchodilator reversibility, and low pretreatment forced expiratory volume in 1 second/forced vital capacity (FEV₁/FVC) when compared with poor (<5%) FEV₁ response. Both BDP and FP caused dose-dependent cortisol suppression.

**Conclusions.** Near-maximum improvements in FEV₁ and methacholine PC-20 occurred with low doses of FP and medium doses of BDP in these subjects with moderate persistent asthma. Higher doses did not improve efficacy but directly increased systemic side effect, as measured by overnight cortisol secretion. When comparing different ICS in future studies, larger numbers of subjects will be necessary to better define dose-response relationships for both efficacy and side effects.
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John M. Kelso
Pediatrics 2003;112;482

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