

# Budesonide and nedocromil did not improve lung function, but budesonide improved symptom control in asthmatic children

The Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. *N Engl J Med.* 2000 Oct 12;343:1054-63.

## QUESTION

In children with asthma, does continuous, long-term treatment with budesonide or nedocromil improve lung function better than treatment for asthma symptoms only?

## DESIGN

Randomized {allocation concealed\*}†, {partially blinded (active treatment vs placebo was blinded, but mode of treatment [steroid vs nonsteroid] was not)}†,\* controlled trial with mean 4.3 years of follow-up.

## SETTING

8 clinical centers in the United States and Canada.

## PATIENTS

1041 children who were 5 to 12 years of age (mean age 9 y, 60% boys), had mild-to-moderate asthma, and had no other clinically significant condition. Follow-up was 98% for the primary outcome and  $\geq 86\%$  for diary card outcomes.

## INTERVENTION

Patients were allocated to 1 of 2 active agents or a matching placebo. Active agents were budesonide, 200  $\mu\text{g}$  twice daily in two 100- $\mu\text{g}$  puffs from a metered-dose inhaler (MDI) ( $n = 311$ ), or nedocromil sodium, 8 mg twice daily in four 2-mg puffs from a pressurized MDI ( $n = 312$ ). Placebos were given to 208 patients (matching budesonide) and 210 patients (matching nedocromil)

## MAIN OUTCOME MEASURES

Lung growth (change in postbronchodilator FEV<sub>1</sub>, expressed as percentage of the predicted value). Secondary outcomes were degree of airway responsiveness to methacholine challenge, symptoms, physical growth, and psychological development.

## MAIN RESULTS

At follow-up, groups did not differ for change in postbronchodilator FEV<sub>1</sub>. Budesonide was better than placebo for improving airway responsiveness; reducing hospitalization rates, urgent-care visits, prednisone use, symptoms, depression, and use of albuterol for symptoms; and increasing episode-free days (Table). Nedocromil was better than placebo for reducing urgent-care visits and courses of prednisone (Table); hospitalization rates were

similar. The mean height increase was 1.1 cm less in the budesonide group than in the placebo group ( $P = 0.005$ ).

## CONCLUSIONS

In children with mild-to-moderate asthma, budesonide and nedocromil did not improve lung function. Budesonide improved airway responsiveness and symptom control.

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*For correspondence: Dr. J. Tonascia, CAMP Coordinating Center, Johns Hopkins University, 615 North Wolfe Street, Room 5010, Baltimore, MD 21205, USA.*

\*See Glossary.

†Information provided by author.

## Budesonide (Bud) or nedocromil (Ned) vs placebo (Pl) for asthma in children

Outcomes at mean 4.3 y	Comparisons	Mean value†	P value
Airway responsiveness (follow-up–baseline ratio)	Bud vs Pl	3.0 vs 1.9	<0.001
Urgent-care visits (number/100 person-y)	Bud vs Pl	12 vs 22	<0.001
	Ned vs Pl	16 vs 22	0.02
Hospitalizations (number/100 person-y)	Bud vs Pl	2.5 vs 4.4	0.04
Prednisone course (number/100 person-y)	Bud vs Pl	70 vs 122	<0.001
	Ned vs Pl	102 vs 122	0.01
Changes in symptom score	Bud vs Pl	-0.44 vs -0.37	0.005
Changes in episode-free days (number/mo)	Bud vs Pl	11.3 vs 9.3	0.01
Changes in albuterol use for symptoms (puffs/wk)	Bud vs Pl	-7.4 vs -5.3	<0.001
Change in total score on Children's Depression Inventory	Bud vs Pl	-3.2 vs -2.2	0.01

†Means are adjusted for baseline measure, age at randomization, ethnic group, sex, clinic, duration of asthma, severity of asthma, and skin-test reactivity.

## COMMENTARY

The Childhood Asthma Management Program Research Group trial is well designed. First, the treatment protocols are flexible, allowing for dose reduction and augmentation. Second, the follow-up was long enough to assess safety and efficacy while avoiding seasonal trends. Third, a 98% follow-up rate for the main outcome at 4 years is outstanding and shows the advantage of doing research in a community-based setting. Fourth, important outcomes were considered. Fifth, the power for detecting small differences was high. However, because of the delivery system, children could not be blinded to the class of drug, only to whether they received active medication or placebo. How well this blinding was maintained is not reported.

A transient decrease in growth velocity occurred primarily in the first year of budesonide treatment, which supports the results of a recent systematic review of beclomethasone in steroid-naïve children (1). At follow-up, predicted final height and bone age were similar in all groups.

To whom can we apply the results? The participants were children with mild-to-moderate chronic asthma who had prebronchodilator

FEV<sub>1</sub> of  $\geq 65\%$  predicted and  $\geq 1$  of the following (80% of children): asthma symptoms  $\geq$  twice weekly or inhaled bronchodilator use  $\geq$  twice weekly, or both; or daily medication use before enrollment. Outcomes from the methacholine challenge indicate chronic asthma.

Should we avoid inhaled budesonide in symptomatic children to avoid the transient decrease in growth velocity? No. Almost 20% of the placebo group received additional inhaled beclomethasone or other asthma treatment drugs. They received 75% more short courses of systemic steroids than did the budesonide group. They were sicker with unsatisfactory asthma control. It is safe to conclude that inhaled budesonide given at the minimal effective dose remains the treatment of choice for children with persistent asthma.

*Francine M. Ducharme, MD, MSc  
McGill University  
Montreal, Quebec, Canada*

## Reference

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