Budesonide and nedocromil did not improve lung function in children with asthma

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

Design

Randomised [allocation concealed*]†, [partially blinded (active treatment *v* placebo was blinded), but mode of treatment [steroid *v* non-steroid] was not)†; * controlled trial with mean 4.3 years of follow up.

Setting

8 clinical centres in the US and Canada.

Patients

1041 children who were 5–12 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 lung function and ≥86% for diary outcomes.

Intervention

Patients were allocated to 1 of 2 active agents or a matching placebo. Active agents were budesonide, 200

µg twice daily in two 100 µg puffs from a metered dose inhaler (MDI) (n=311), or nedocromil sodium, 8 mg twice daily in four 2 mg puffs from a pressurised MDI (n=312). Placebos were given to 208 patients (matching budesonide) and 210 patients (matching nedocromil).

Main outcome measures

Lung growth (change in postbronchodilator FEV₁). 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 FEV₁. Budesonide was better than placebo for improving airway responsiveness; reducing hospitalisation 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); hospitalisation 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.

*See glossary.

†Information provided by author.

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Budesonide (Bud) or nedocromil (Ned) *v* placebo (P) for asthma in children ‡

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

† Means are adjusted for baseline measure, age at randomisation, 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. Firstly, the treatment protocols are flexible, allowing for dose reduction and augmentation. Secondly, the follow up was long enough to assess safety and efficacy while avoiding seasonal trends. Thirdly, 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. Fourthly, important outcomes were considered. Fifthly, 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 naive 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 FEV₁ of ≥65% predicted and ≥1 of the following (80% of children): asthma symptoms ≥ twice weekly or inhaled bronchodilator use ≥ twice weekly, or both; or daily medication use before enrolment. Outcomes from the methacholine challenge indicate that the children had 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 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.

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1 Sharek PJ, Bergman DA. Beclomethasone for asthma in children: effects on linear growth. *Cochrane Database Syst Rev* 2001;(1):CD001282.