

# Growth rate was greater with fluticasone propionate than with beclomethasone dipropionate in children with chronic asthma

de Benedictis FM, Teper A, Green RJ, et al., for the International Study Group. Effects of 2 inhaled corticosteroids on growth. Results of a randomized controlled trial. Arch Pediatr Adolesc Med. 2001 Nov;155:1248-54.

## QUESTION

In children with chronic asthma, what are the effects of fluticasone propionate compared with those of beclomethasone dipropionate on growth rates?

## DESIGN

Randomized (allocation concealed\*), blinded (unclear),\* controlled trial with 12-month follow-up.

## SETTING

32 centers in 7 countries: the Netherlands, Hungary, Italy, Poland, Argentina, Chile, and South Africa.

## PATIENTS

343 children who were 4 to 11 years of age (mean age 8 y, 72% boys); had a sexual maturity rating of Tanner stage 1; required treatment with fluticasone propionate, 100 to 200 µg/d, or beclomethasone dipropionate or budesonide, 200 to 500 µg/d, for ≥ 8 weeks before study entry at a constant dosage for ≥ 4 weeks before the run-in period; had a mean morning peak expiratory rate (PEFR) during the last 7 days of the run-in period of ≤ 85% of their maximum achievable response after using a metered-dose inhaler containing albuterol sulfate, 400 µg;

and had an asthma symptom score ≥ 1 or required albuterol ≥ 1 time daily on ≥ 4 days during the last 7 days of the run-in period. Exclusion criteria were intermittent asthma or disorders that could affect growth, receipt of oral or parenteral steroids, or hospitalization with respiratory disease in the 4 weeks before the run-in period. 81% of patients were included in the analysis for growth rate.

## INTERVENTION

After the 2-week run-in period, during which patients continued to receive their existing inhaled corticosteroid treatment and albuterol sulfate on an as-needed basis, they were allocated to inhaled fluticasone propionate, 200 µg twice daily ( $n = 170$ ), or beclomethasone dipropionate, 200 µg twice daily ( $n = 173$ ), by dry-powder inhaler for 52 weeks.

## MAIN OUTCOME MEASURE

Change in height (growth rate) as measured by stadiometry.

## MAIN RESULTS

Patients ( $n = 277$ ) with ≥ 2 data points (at randomization and on or after 16 wk of treatment) who did not reach a Tanner stage of ≥ 2 during the study and who did not have other factors that would probably affect the measurement of growth (e.g., poor compliance or use of systemic corticosteroids) were included in the analysis. Adjusted mean growth rate was greater in the fluticasone group than in the beclomethasone group (Table).

## CONCLUSION

The growth rate of children with chronic asthma was greater with fluticasone propionate than with beclomethasone dipropionate.

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\*See Glossary.

## Fluticasone propionate vs beclomethasone dipropionate in children with chronic asthma†

Outcome at 12 mo	Fluticasone	Beclomethasone	Difference in mean change (95% CI)
Increase in height (cm/y)	5.01	4.10	0.91 (0.63 to 1.20)

†Adjusted for height and age at randomization, grouping by country, sex, and ethnicity.

## COMMENTARY

The well-designed study by de Benedictis and colleagues addressed an important question and showed that at 12 months, children with chronic asthma treated with fluticasone were about 1 centimeter taller than those treated with beclomethasone. Children treated with fluticasone showed better lung function than did those treated with beclomethasone (adjusted mean PEFR 282.5 vs 267.3 L/min,  $P < 0.001$ ), but groups did not differ for asthma symptom scores, use of rescue albuterol, exacerbations, or adverse events (including assessment of adrenal axis function, although follow-up was < 80% for this outcome). However, the study was not powered to show equivalence for these outcomes.

The primary analysis assesses the efficacy of treatment for asthma and how it affects growth rate. The intention-to-treat analysis gives similar, although less striking, results (difference in means 0.7 cm/y, 95% CI 0.13 to 1.26, in favor of fluticasone). Thus, we can safely conclude that fluticasone, 400 µg/d, was associated with a greater growth rate than was the same dose of beclomethasone.

How can we explain the difference in growth rates? One obvious reason may be the drugs themselves, in part because of a difference in sys-

temic bioavailability. Another reason may be the enhanced asthma control achieved in the fluticasone group. The unanswered question is whether the results for growth rate continue to hold true when equivalent drug potency is addressed; at a 2:1 ratio for potency, children treated with fluticasone propionate, 400 µg/d, received twice as much anti-inflammatory medication than did those treated with beclomethasone dipropionate, 400 µg/d. If the drug is responsible for the effect on growth, fluticasone will have a lesser effect on growth than an equipotent dose of beclomethasone of 800 µg/day. Will this effect be annihilated by enhanced lung function and asthma control achieved in children treated with beclomethasone, 800 µg/d? Such a comparison would better address whether the drug itself or asthma control is responsible for the difference in growth between groups. Until then, what should we do? In children whose asthma is not well controlled with beclomethasone, 400 µg/d, a switch to fluticasone, 400 µg/d, with tapering to the minimal effective dose would be an interesting option.

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