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Treatment of mild persistent asthma in children

Fernando Martinez and co-workers (Feb 19, p 650)¹ highlight that daily use of inhaled corticosteroids is associated with reduced growth, and that intermittent use of these drugs to control mild persistent asthma avoids such growth impairment. This statement could lead physicians and (parents of) patients to think that daily inhaled corticosteroid treatment is unsafe and stunts growth. I would like to point out that the currently available evidence does not support a clinically relevant effect on long-term growth of inhaled corticosteroid therapy in children.

The effects of inhaled corticosteroids on growth have been extensively studied and reviewed.2 Although low to moderate doses (<400 µg per day budesonide or equivalent) are associated with a reduction of growth in height during the first year of treatment of 1-2 cm, this effect does not accumulate over further years of treatment.³ Studies that have followed up children on inhaled corticosteroids for many years into adulthood consistently show normal adult attained height,⁴ probably because these children grow for longer than their peers and reach normal adult height at a slightly later age.⁵ Thus, inhaled corticosteroids seem to reset the growth clock temporarily, after which normal growth recurs and remains.

In my opinion, it is therefore inappropriate to use the expected slight growth reduction in the first year of inhaled corticosteroid treatment as an argument against long-term maintenance treatment with such drugs, because the long-term growth of children who use these compounds for many years is normal.

I declare that I have no conflicts of interest.

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Princess Amalia Children's Clinic, PO Box 10400, 8000 GK Zwolle, Netherlands Martinez FD, Chinchilli VM, Morgan WJ, et al. Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial. *Lancet* 2011; **377:** 650–57.

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- Leone FT, Fish JE, Szefler SJ, West SL. Systematic review of the evidence regarding potential complications of inhaled corticosteroid use in asthma: collaboration of American College of Chest Physicians, American Academy of Allergy, Asthma, and Immunology, and American College of Allergy, Asthma, and Immunology. *Chest* 2003; **124**: 2329–40.
- Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. N Engl J Med 2000; **343:** 1054-63.
- Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. N Engl J Med 2000; **343:** 1064–69.
- 5 Pedersen S. Do the benefits of daily inhaled steroid treatment of mild asthma outweigh the risks? Arch Dis Child 2008; **93:** 644-45.

In their randomised controlled study of children with mild persistent asthma, Fernando Martinez and colleagues¹ show that regular inhaled steroids plus use of combined inhaled steroids plus salbutamol for rescue use is best at reducing and preventing excacerbations (measured by treatment failure). They conclude that "the most effective treatment to prevent exacerbations is daily inhaled corticosteroids". However they, and in his accompanying Comment, William Checkley,² imply that inhaled corticosteroids as rescue medication with albuterol/salbutamol might be useful for treating these children.

Although this rescue approach is a concept that has become accepted and criticised³ after studies in adults using the so called Symbicort SMART Regime,⁴ the suggestion that this form of treatment might be useful in children is worrying, because of Martinez and colleagues' findings. Although, compared with placebo, there were fewer exacerbations and episodes of "treatment failure" in the rescue group, the bottom line is that more than a third of patients prescribed the rescue medication had exacerbations and nearly 10% were deemed to have "treatment failure".

These data cannot be used to advocate this rescue approach for

managing children with mild, persistent asthma, and I would be surprised if further research secures ethics approval on the basis of these data. As Martinez and colleagues state, the best treatment for these patients with mild persistent asthma is regular inhaled steroid, and that is what the current international asthma strategy states.⁵

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- Martinez FD, Chinchilli VM, Morgan WJ, et al. Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial. Lancet 2011; 377: 650–57.
- 2 Checkley W. New insights into the treatment of persistent asthma. *Lancet* 2011; **377:** 614–16.
- 3 Chapman KR, Barnes NC, Greening AP, Jones PW, Pedersen S. Single maintenance and reliever therapy (SMART) of asthma: a critical appraisal. Thorax 2010; 65: 747–52.
- 4 Demoly P, Louis R, Soes-Petersen U, et al. Budesonide/formoterol maintenance and reliever therapy versus conventional best practice. *Respir Med* 2009; **103**: 1623–32.
- Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2010. http://www.ginasthma.org/ Guidelineitem.asp??l1=2&l2=1&intld=60 (accessed March 3, 2011).

Fernando Martinez and colleagues¹ report the use of rescue inhaled corticosteroids plus salbutamol in mild persistent asthma. We agree with them as regards the necessity of minimising treatment with inhaled corticosteroids, but we would like to focus on step-down therapy.

This strategy, according to guidelines,² often implies a slow tapering of Submissions should be made via our electronic submission system at http://ees.elsevier.com/ thelancet/