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Inhaled glucocorticoid use produces a small but important impact on adult height

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ABSTRACT A critical appraisal and clinical application of: Kelly HW, Sternberg AL, Lescher R, et al. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012;367(10):904-912. doi:[10.1056/NEJMoa1203229](https://doi.org/10.1056/NEJMoa1203229).
Keywords: childhood asthma, inhaled corticosteroids, adult stature

Clinical Context

A six-year-old asthmatic child presented to the clinic after an emergency room visit for an acute asthma exacerbation. Upon further questioning, it was disclosed that prior to the emergency room visit, the child both required albuterol treatments more than twice weekly and had interrupting nighttime symptoms that occurred more than once per month. Based on this presentation, the patient was categorized as an uncontrolled persistent asthmatic and, according to standard clinical guidelines, was instructed to initiate daily inhaled corticosteroid therapy.

Clinical Question

What is the effect of inhaled glucocorticoids during childhood on adult height?

Research Article

Kelly HW, Sternberg AL, Lescher R, et al. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med* 2012; 367(10):904-912. doi:[10.1056/NEJMoa1203229](https://doi.org/10.1056/NEJMoa1203229).

Literature Review

Multiple studies have shown that there is a clear reduction in growth velocity in persistent asthmatic children, especially upon prepubertal initiation of an inhaled glucocorticoid.¹ However, the majority of studies that have been done to evaluate a permanent reduction in adult height have either noted no difference or a small difference in predicted and attained adult height in these children.¹⁻³

A small prospective study done in 1996 (N=332) was of limited value because there were 59 participants lost to follow-up, nine participants had missing data, 97 participants had not yet reached adult height, 34 participants crossed over to the inhaled corticosteroid group, and 7 participants took oral steroids. This left only 18 participants in the comparator group.²

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In a case-controlled study done in 1996 ($N=306$), which was controlled for mid-parental height, the authors concluded that there was no permanent impact on achievement of adult height. The study depended on poorly described methods of chart review to identify subjects, which limited its validity.

A meta-analysis of 95 articles done in 1994 compared attained heights to expected heights in patients exposed to steroids. The authors concluded that there was a small but significant tendency of corticosteroid therapy to be associated with diminished final height, but that overall, inhaled use of corticosteroids did not significantly impact stature.

Critical Appraisal

The Childhood Asthma Management Program trial is designed to determine the benefits of an inhaled corticosteroid in persistent asthmatics.⁴ The article under review, written by Kelley, et al. (SORT Level of Evidence: 2), is a secondary analysis of the original CAMP Trial data. Kelley, et al. compare height differences between asthmatics treated with inhaled budesonide, inhaled nedocromil, or placebo. After the first four-to-six years, the participants were followed into adulthood to measure their attained heights. During the first four-to-six years, protocol adherence was good: 636.1 mg glucocorticoid dose in the budesonide group, 88.5 mg in the nedocromil group, and 109.4 mg in the placebo group. At that time, researchers reported a significant difference in participants' heights that persisted into adulthood. They also reported a difference between the inhaled corticosteroid group and the placebo group: 1.2 cm shorter 95% CI [-1.9 to -0.5 cm], ($p=0.0010$). However, after the initial phase, glucocorticoid use equalized between the three groups: 381 mg, 347 mg, and 355 mg, respectively. Therefore, the authors' conclusion that there is no progressive loss of adult height is not supported.

This randomized trial, which includes the important outcome variable of adult height, is relevant because clinicians frequently encounter patients such as those enrolled in the study and are called upon to advise parents regarding the risk of harm versus benefit for inhaled glucocorticoids in asthmatic children. During the study, follow-up was excellent and patients were analyzed according to the group into which they were randomized. Because the inhalation devices may have been distinguishable to the participants, the study lacked strong blinding protocols. Otherwise, the groups were treated equally. The limitations of the study include the investigation of a single agent, budesonide, without consideration of any other corticosteroids, and administration of a single dose, 200 ug twice daily, instead of the now recommended dose of 200 ug once daily. The study may have yielded more useful clinical applications had the authors administered a lower dose of budesonide or included alternative corticosteroids.

Clinical Application

In the clinic, the primary care team explained to the parents that daily inhaled corticosteroid use may cause a reduction in adult height, about 1 cm or more, with continued use. The parents were dismissive of this information; they thought the benefit of keeping their child out of the hospital and controlling the asthma episodes were far greater concerns than was a small height loss.

The primary care team learned that despite the seemingly authoritative claims of Kelley, et al., there is still some uncertainty about the effects of inhaled glucocorticoid therapy in an asthmatic child with regard to his/her adult height. For the care of future, similar patients, we believe shared decision-making between physician and parent(s) should include a discussion of the potential impact of continued glucocorticoid use on a child's adult height. Socially and culturally speaking, height is considered a desirable physical trait; while 1 cm of height loss may seem trivial to one person, it may be an unacceptable consequence to another. If the parent or the child has a shorter stature and does not want to risk further height deficiencies, this information might impact therapeutic choices.

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