A meta-analysis of the effect of oral and inhaled corticosteroids on growth

Allen D B, Mullen M, Mullen B

Authors' objectives
To assess the effect of inhaled and oral corticosteroids on linear growth, i.e. height.

Searching
The authors state that an ‘exhaustive literature search of leading medical journals’ was performed from 1956 to 1993, although the actual sources were not stated.

Study selection
Study designs of evaluations included in the review
Studies using qualitatively different measurements of growth such as knemometry, and those using parametric statistics to analyse average heights, were excluded. Any remaining study capable of supplying the outcomes information appears to have been included.

Specific interventions included in the review
The specific corticosteroids were grouped into 3 classes: inhaled beclomethasone dipropionate (BDP), oral prednisone, and ‘other’ oral corticosteroids. BDP daily dosages ranged from 200 to 875 mg.

Participants included in the review
Patients with asthma were included. The mean age of patients in the primary studies ranged from 7.5 to 12.5 years.

Outcomes assessed in the review
The number of patients with asthma receiving corticosteroids who were at and above, or below their height for their age, was extracted from each study.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Product-moment correlations (r) were obtained for each study based on the numbers of patients at and above, or below their expected height for their age, and corticosteroid use. A mean ‘r’ was then calculated to estimate an overall effect size. Further analyses also examined the influence of patient age, therapy duration, dosage, and illness severity on the effect of BPD on growth.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.
Results of the review
Twenty-one studies comprising a total of 810 patients were included.

General effect: there was a significant but small tendency for corticosteroid therapy to be associated with being shorter than one’s expected height (Z=2.328, p=0.0100, mean r=-0.023). The effect varied with the type of drug used: oral prednisone was significantly associated with decreased height (Z=2.137, p=0.0164, r=-0.295), BDP with normal stature (Z=7.395, p=2.17E-13, mean r=0.432), and ‘other’ oral corticosteroids showed a significant but weak association with reduced height (Z=9.107, p=2.44E-18, mean r=-0.260). Any growth-retarding effect of BDP appeared to be age-related: the correlation (r) between the size of BDP’s effect on growth and patient age was -0.568 (Z=4.058, p=0.0000249). The predicted BDP-growth effect was calculated to be zero at age 11.2 years, indicating a cut-off point beyond which inhaled BDP was more likely to cause growth impairment.

Effects of therapy duration: greater duration of BDP therapy was associated with no growth impairment. (Z=1.977, r=0.273, p=0.0240). This lack of association remained when the effects of age were taken into consideration.

Effects of dosage: increased dosage of BDP was associated with an absence of growth impairment (Z=2.144, r=0.263, p=0.0160).

Effects of illness severity: greater dosages of BDP tended to be used in more severe cases though the trend was not significant (p=0.159). Patients with severe asthma showed a significantly weaker positive effect for attaining normal stature (Z=2.318, p=0.0102) than those with less severe asthma. Overall, however, there did not appear to be any significant associations between growth impairment and any combination of illness severity and BDP dosage. The number of studies reporting no effect, which would render the meta-analysis non significant, has been calculated by the authors: 2 studies reporting no general effect of therapy on growth would be required.

Authors’ conclusions
There is a significant but weak association between corticosteroid use and growth impairment, which is dependent on the drug used, such that prednisone and ‘other’ corticosteroids are associated with impairment and BDP with normal growth. For BDP, growth impairment is slightly more likely after 11 years of age. Prolonged BDP therapy is not associated with any increased risk, and there is no evidence of greater growth impairment with higher dosages of BDP, as used in more severe illness. However, the growth-retardant effect of dosages higher than currently recommended levels remains uncertain.

CRD commentary
The low fail-safe number calculated by the authors raises the question as to whether a more formal search strategy, which included searches of electronic databases, would find additional studies and thus produce different conclusions. Similarly, given this low fail-safe number, the size of the effect is also likely to be sensitive to different study inclusion criteria. The main finding of this meta-analysis, regarding the general effect of corticosteroids on growth, therefore lacks robustness. However, the fail-safe numbers reported for the effect of specific drugs and patient age are sufficiently large.

Another drawback of this review is the limited consideration of the role of potential confounding variables. It should also be noted that the results relating to patient age, therapy duration, dosage and illness severity apply to BDP therapy only.

Bibliographic details
Allen D B, Mullen M, Mullen B. A meta-analysis of the effect of oral and inhaled corticosteroids on growth. Journal of Allergy and Clinical Immunology 1994; 93(6): 967-976

PubMedID
8006318
Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Inhalation; Administration, Oral; Adrenal Cortex Hormones /administration & dosage /adverse effects; Age Factors; Asthma /drug therapy; Beclomethasone /adverse effects; Child; Growth /drug effects; Humans

AccessionNumber
11995003418

Date bibliographic record published
31/07/1996

Date abstract record published
31/07/1996

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.