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ADVANCES IN PEDIATRICS

Effects of Inhaled Corticosteroids on Growth, Bone Metabolism, and Adrenal Function

Peter M. Wolfgram, MD[a], David B. Allen, MD[b,*]

[a]Department of Pediatrics, Medical College of Wisconsin, CCC540, 9000 W. Wisconsin Avenue, Milwaukee, WI 53226, USA; [b]Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, H4/448 CSC–Pediatrics, 600 Highland Avenue, Madison, WI 53792-4108, USA

Keywords

• Asthma • Corticosteroids • Pediatrics • Growth • Adrenal function • Bone mass

Key points

- Inhaled corticosteroids are first-line therapy for persistent asthma in children.
- Major safety concerns of long-term inhaled corticosteroid therapy include suppression of adrenal function, growth, and bone development.
- Proper interpretation of inhaled corticosteroid safety studies requires knowledge of differences between various inhaled corticosteroid drug/delivery device systems.
- Dosage, type of inhaler device used, patient technique, and characteristics of the individual drug influence efficiency of drug delivery to the lungs and, therefore, systemic exposure to inhaled corticosteroid.
- Systemic side effects can occur when continuous high-dose treatment is required for severe asthma or when the prescribed dose is excessive and medication compliance unusually good.
- In addition, with regard to growth, concomitant use of other medications with potential growth-suppressing effects, can influence the magnitude of adverse effect.
- Overall, however, studies confirm that benefits of inhaled corticosteroids, properly prescribed and used, clearly outweigh not only their potential adverse effects, but also the risks associated with poorly controlled asthma.

*Corresponding author. *E-mail address:* dballen@pediatrics.wisc.edu

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INTRODUCTION

Asthma is the most common chronic inflammatory disease of children, and inhaled corticosteroids (ICS) are the most effective and commonly used treatment of persistent asthma. ICS currently approved for and commonly used by children with asthma include beclomethasone dipropionate (BDP), budesonide (BUD), fluticasone propionate (FP), mometasone furoate, ciclesonide (CIC), and triamcinolone acetonide. This report reviews recently published information in 4 areas critical to understanding the literature on adverse effects of ICS and placing them in proper perspective: (1) influence of drug/delivery device properties on systemic steroid burden, (2) reports and causes of adrenal insufficiency during ICS treatment, (3) growth effects of ICS and asthma itself, and (4) bone mineral accretion during ICS therapy. For background information and references, the reader is referred to comprehensive reviews [1–4].

IMPORTANT DIFFERENCES IN INHALED CORTICOSTEROID CHARACTERISTICS, DELIVERY, AND ABSORPTION

A challenge in properly interpreting studies of ICS safety is assessing whether clinically equivalent drug/delivery device regimens are being compared. The potency of specific ICS preparations varies widely; judged according to glucocorticoid-receptor binding affinity, the relative topical potencies of ICS are FP > momentasone furoate > desisobutyryl-ciclesonide (DES-CIC; desisobutyryl-ciclesonide is the active metabolite of ciclesonide) BUD > beclomethasone-17-monoproprionate (BMP; beclomethasone monopropionate is the active metabolite of beclomethasone dipropionate) > triamcinolone acetonide. The amount of systemic absorption depends not only on the actual dose administered but also on the mode of delivery. Although most dry powder inhalers (DPI) and nebulizers generally deliver only 10% to 30% of the nominal dose to the lung, hydrofluoroalkane (HFA)-propelled metered dose inhalers (MDI), which have replaced ozone-depleting chlorofluorocarbon (CFC)-propelled MDIs, deliver up to 56% of the nominal dose to airways [4]. The addition of a spacer device to an MDI can further increase the percentage of the nominal dose reaching the lungs by up to 20%. After inhalation, the portion of drug that reaches the lungs exerts therapeutic anti-inflammatory effects before essentially complete absorption into the systemic circulation. In contrast, drug swallowed and absorbed exerts systemic effects without substantial organ-specific anti-inflammatory effects [1].

Although various ICS preparations are thought to have similar clinical efficacy when used at equivalent therapeutic doses, differences in pharmacokinetics affect their safety profiles. The percentage of drug systemically available after oral administration varies greatly, estimated to be less than 1% for FP, momentasone furoate, and CIC but up to 41% for BDP, 23% for triamcinolone acetonide, and 10% for BUD (Fig. 1) [4–6]. Thus, clinically relevant differences in the ratio of drug absorbed through the lungs to total drug absorbed into the systemic circulation primarily reflects differences in gastrointestinal absorption and first-pass hepatic metabolism. Other important drug