Original Article

Small-particle Inhaled Corticosteroid as First-line or Step-up Controller Therapy in Childhood Asthma

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What is already known about this topic? Evidence from randomized controlled trials regarding asthma controller therapies for children is limited, usually short-term, and often not generalizable to general practice, where most children with asthma are managed.

What does this article add to our knowledge? Over 1 outcome year, small-particle inhaled corticosteroid (ICS) was more effective than standard size–particle ICS for children initiating or stepping up ICS therapy and as effective as adding a long-acting β_2-agonist in a fixed-dose combination inhaler.

How does this study impact current management guidelines? These findings challenge asthma guidelines that recommend adding a long-acting β_2-agonist as the first-line alternative for stepping up therapy when asthma is not controlled by ICS monotherapy.

BACKGROUND: Because randomized controlled trials of established pediatric asthma therapies are expensive and difficult to perform, observational studies may fill gaps in the evidence base.
OBJECTIVES: To compare the effectiveness of representative small-particle inhaled corticosteroid (ICS) with that of standard size–particle ICS for children initiating or stepping up ICS therapy for asthma (analysis 1) and to compare the effectiveness of ICS dose step-up using small-particle ICS with adding long-acting β_2-agonist (LABA) to the ICS (analysis 2).
METHODS: These historical matched cohort analyses drew on electronic medical records of children with asthma aged 5 to 11 years. Variables measured during 2 consecutive years (1 baseline year for confounder definition and 1 outcome year) included risk-domain asthma control (no hospital attendance for asthma, acute oral corticosteroids, or lower respiratory tract infection requiring antibiotics) and rate of severe exacerbations (asthma-related emergency, hospitalization, or oral corticosteroids).
RESULTS: In the initiation population (n = 797 in each cohort), children prescribed small-particle ICS versus standard size–particle ICS experienced greater odds of asthma control (adjusted odds ratio, 1.49; 95% CI, 1.10-2.02) and lower severe exacerbation rate (adjusted rate ratio, 0.56; 95% CI, 0.35-0.88). Step-up outcomes (n = 206 in each cohort) were also significantly better for small-particle ICS, with asthma control adjusted odds ratio of 2.22 (95% CI, 1.23-4.03) and exacerbations adjusted rate ratio of 0.49 (95% CI, 0.27-0.89). The number needed to treat with small-particle ICS to achieve 1 additional child with asthma control was 17 (95% CI, 9-107) for the initiation population and 5 (95% CI, 3-78) for the step-up population. Outcomes were not significantly different for stepped-up small-particle ICS dose versus ICS/LABA combination (n = 185 in each cohort).
CONCLUSIONS: Initiating or stepping up the ICS dose with small-particle ICS rather than with standard size–particle ICS is more effective and shows similar effectiveness to add-on LABA in childhood asthma. **(J Allergy Clin Immunol Pract 2015;■:■-■)**

Key words: *Asthma; Childhood; Small-particle beclomethasone; Fluticasone; Inhaled corticosteroid; Long-acting β_2-agonist; Step-up therapy*

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Abbreviations used
adjOR- adjusted odds ratio
adjRR- adjusted rate ratio
GP- general practice
ICS- inhaled corticosteroid
LABA- long-acting β_2-agonist
NNT- number needed to treat
pMDI- pressurized metered-dose inhaler
RCT- randomized controlled trial
SABA- short-acting β_2-agonist

Clinicians managing children with asthma in community settings, where most patients with asthma are seen, must rely on evidence for their therapeutic choices primarily from randomized controlled trials (RCTs). However, funding for large independent RCTs is limited; moreover, RCT results may not be widely generalizable to unselected patient populations. They exclude many children with asthma who have intermittent, milder disease and who may be most prone to exacerbations. In addition, RCTs seldom include comparisons of step-up strategies, directly compare different types or formulations of inhaled corticosteroids (ICS), or provide the long-term comparisons (>12 weeks) needed for evaluating infrequent events, such as exacerbations.[1-5] Head-to-head RCTs are challenging to institute because of difficulties in unravelling the roles of corticosteroid potency, initial dose from different inhaler devices, and delivered dose to the lower airways. Moreover, recruitment into RCTs of children with poor control sufficient to justify a change in therapy is notoriously very difficult.[6] Finally, the enforced adherence to prescribed medication in RCTs is difficult to duplicate in clinical practice, further limiting the applicability of RCT results.

Information from observational studies of pediatric asthma therapies can complement the limited evidence currently

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