

Use of Systemic Corticosteroids in Children with Asthma: Evidence of Treatment of Failure and Future Risk



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The paper by Sullivan and colleagues¹ in this issue of the *Journal* addresses the associated complications and increases in health care resources utilization (HCRU) observed with systemic corticosteroids (SCS) use in children with asthma. When multiple bursts of SCS are prescribed, there is an amplified risk for complications and HCRU. Systemic corticosteroids are the standard of care for treating severe exacerbations of asthma in children who are unresponsive to increased inhaled bronchodilator containing medications; once prescribed, the clinical episode is defined as a severe asthma exacerbation.² Furthermore, the use of SCS for severe asthma worsening is a primary predictor of the future risk for a severe exacerbation, a critical complication of asthma.^{3,4}

The current paper uses MarketScan, a large claims database from commercial payers, that reports HCRU and pharmacy claims. This study confirms the present and future risk associated with SCS, including asthma-related emergency department visits and hospitalizations. The paper identifies children whose asthma treatments failed to prevent exacerbations requiring SCS. Claims data have the potential to alert providers to initiate clinical assessment to revise asthma management and prevent future treatment failures requiring SCS. The ability to recognize at-risk children with claims databases is enhanced when paired with the electronic health record. Together, they can assess whether prescribed medications are dispensed, provide the clinical context to assess the appropriateness of the therapy, and be used to alert providers with recommendations for additional or alternative therapies.

Claims databases have strengths and limitations. They provide insight into associations between a therapeutic intervention and the benefits and risks of the treatment. The power of these associations is strengthened by the large number of patients studied. They are limited in their ability to demonstrate cause and effect. To address this constraint in this study, propensity matching was used to establish a comparable control group. The suitability of this statistical technique is addressed in the paper¹ as well as in the review by Reiffel.⁵ Sullivan and colleagues¹ performed propensity matching employing demographic data, the Charlson Comorbidity index, a categorical definition for high

and low (≥ 7 and < 7 canisters/y) beta-agonist use, and health care use. The propensity matching was limited by the lack of access to additional clinical variables such as spirometry, immunoglobulin E values, dosage of inhaled corticosteroids (ICS), total eosinophil counts, exhaled NO, ethnicity, and socioeconomic factors. These variables may have provided further determination of disease severity or an enhanced assessment of total corticosteroids exposure (both inhaled and systemic). The conclusion of this observational report, that the use of SCS is associated with greater complications and increased HCRU, is confounded by the correlation of severe uncontrolled asthma with increased complications, higher HCRU, and the requirement of SCS use. Irrespective of this limitation, identifying SCS use in children should focus on the potential need for further clinical assessment and altered treatment strategy.

The clinical value of SCS in the treatment of severe exacerbations of asthma is well documented. Treatment with SCS may reduce the need for subsequent hospitalization, provide the child with relief from symptoms of worsening asthma, and allow the child to return to school and the parent to work. Compared with using a daily controller, multiple short bursts of SCS therapy can be deceptively and inappropriately perceived as less burdensome to the child and caregiver. However, data from Sullivan and colleagues¹ confirm that the use of SCS comes at a high burden to the child of an increased risk for asthma worsening and complications of both the disease and the treatment. This paper highlights that the use of SCS should be considered a warning to the provider, patient, and caregiver of potential limitations in the child's current asthma therapy to prevent severe exacerbations.

Children with claims for SCS to treat asthma exacerbations may benefit from an additional evaluation to determine the etiology of the uncontrolled asthma. A detailed history and biological and physiological assessments are needed to define the asthma phenotype. This clinical evaluation should assess whether the prescribed treatment is appropriate, and confirm that the child has access to the therapy, is adherent to the medications, and has an acceptable inhalation technique. The treatment plan should include patient and family asthma education and an understanding of the rationale for the prescribed treatment. An action plan to be used during worsening symptoms should provide step-up strategies.^{6,7} In addition, consideration of additional medications including biologics may be warranted. Patient and caregiver understanding and involvement are an important part of the shared decision-making process.

Data on the complications associated with SCS treatment and those associated with greater disease severity may be incompletely addressed by propensity matching. Adverse effects of SCS include immediate, short-term symptoms such as nausea,

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Conflicts of interest: D. A. Stempel is a consultant to Propeller Health and owns stock in its parent company ResMed.

Received for publication January 4, 2021; accepted for publication January 7, 2021.

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J Allergy Clin Immunol Pract 2021;9:1552-3.
2213-2198

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<https://doi.org/10.1016/j.jaip.2021.01.002>

vomiting, and irritability observed during administration of SCS and delayed, long-term adverse effects such as growth velocity-slowness and adrenal insufficiency. Growth retardation is a well-documented long-term adverse event linked to the use of SCS, but it is also associated with chronic illnesses such as childhood asthma. The impact of SCS is confounded by the presence and severity of the chronic disease. This was the subject of an editorial by Elliot Ellis over 30 years ago, noting that “frequent short courses” of SCS were associated with growth velocity slowing.⁸ In addition, he observed that uncontrolled asthma produced greater slowing of growth velocity compared with low-dose alternate day SCS. The literature has more recently focused on potential growth velocity slowing most commonly noted with higher-dose ICS.⁹

Asthma guidelines recommend medium-to high-dose ICS in steps 4 through 6 for children.^{6,7} The literature is limited supporting the risk–benefit ratio of medium to high doses of ICS in children. The Global Initiative for Asthma acknowledges that most of the “clinical benefit is seen at low doses” and that high doses are “arbitrary” and associated with an increased risk for side effects.⁶ Although the Global Initiative for Asthma provides these warnings, its step-care guide defaults to higher doses at higher steps. Databases such as the one employed in this study might be used to determine whether there is clinical evidence for the use of higher doses of ICS or whether the addition of dual inhaled bronchodilators to low-dose ICS or advancing to biologics before increasing the dose of the ICS may reduce corticosteroid complications and provide enhanced asthma control. Having the baseline ICS dosage included in the propensity matching may enable more robust analyses.

Although one may question some of the analytics of the article by Sullivan and colleagues,¹ the paper unmistakably identifies the risk for serious adverse events in children with frequent SCS use and associated high HCRU. It highlights the

importance of using claims databases to identify frequent users of SCS, children who are treatment failures, who would benefit from a more detailed evaluation of asthma. Treating severe exacerbations of asthma with SCS is appropriate and potentially lifesaving. Reducing the frequency of severe exacerbations, though, is the goal and focus of care. For health care providers who prescribe multiple courses of SCS in children, whether in primary or specialty care, this paper should alert them that a comprehensive assessment and potential enhancements to the treatment plan are needed.

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