Things We Do for No Reason™: Systemic Corticosteroids for Wheezing in Preschool-Aged Children

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CASE PRESENTATION

A four-year-old girl, with a history of one wheezing episode, presents to the emergency department (ED) with wheezing, tachypnea, and respiratory distress. She receives three successive treatments of short-acting bronchodilators and is given one dose of dexamethasone, after which she improves significantly. Because of persistent tachypnea and wheezing, she is admitted for further management. By the next day she is much improved, now requiring bronchodilator treatment every four hours. She receives a second dose of dexamethasone to complete her steroid burst. Was the trajectory of this patient's illness altered by treatment with systemic corticosteroids (SCS)? Is there any benefit to SCS treatment in a wheezing preschool-aged patient?

BACKGROUND

Wheezing is common in preschool-aged children (ages 2-5 years), with up to half in this age group having experienced a wheezing episode and up to one-third, recurrent wheezing.[1,2] Young children with wheezing require ED visits and hospitalizations at much higher rates than older children and adults.[3] Several studies have also demonstrated that children in this age group have higher rates of SCS prescriptions compared with older children.[4,5] Despite the high prevalence of wheezing in this age group, there is great heterogeneity in the etiology and clinical progression of early childhood wheezing, with up to six described phenotypes each with varying levels of association with the development of asthma.[6] Given the high frequency of asthma, preschool-aged children admitted with wheezing are often treated with SCS, as this is the standard of care for an acute asthma exacerbation.[7]

WHY YOU MIGHT THINK SYSTEMIC CORTICOSTEROIDS WOULD BE HELPFUL IN TREATING PRESCHOOL WHEEZE

The benefit of SCS in school-aged children and adolescents with multitrigger asthma exacerbation is well established and includes shorter time to resolution of acute illness and reduction in relapses.[8] Because of these benefits, expert panels and regulatory agencies often include preschool-aged children in treatment recommendations for the older age groups.[7,9,10] Consequently, apart from infants diagnosed with bronchiolitis, SCS remain a common and accepted treatment for young children presenting with asthma-like symptoms.[4,5]

Some data suggest that there may be clinical benefit from treatment with SCS in preschool children who wheeze. A recent trial by Foster et al. included 605 children, aged 24-72 months, presenting to a pediatric ED with wheeze plus viral upper respiratory symptoms.[11] Patients were randomized to receive a three-day course of prednisolone (1 mg/kg) or placebo. The primary outcome was length of hospital stay until ready for discharge, which they found was significantly longer for placebo-treated patients (540 minutes) versus prednisolone (370 minutes).

WHY SYSTEMIC CORTICOSTEROIDS ARE NOT ROUTINELY HELPFUL IN PRESCHOOL CHILDREN WHO WHEEZE

There are few randomized controlled trials evaluating the efficacy of SCS in preschool-aged children with viral-induced wheezing, and these children are often grouped with younger or older children in studies. While limited in number, these studies have evaluated SCS efficacy with acute wheezing in preschool-aged children in outpatient, ED, and inpatient settings (Appendix Table).[12-16] The majority of trials of SCS in this age group have shown mixed or negative results.

Admission rates for preschoolers with viral wheezing were not statistically different in those receiving oral prednisolone versus placebo in a study conducted by Oomen et al. evaluating outpatient, parent-initiated prednisolone.[14] Tal et al. found overall benefit with reduced admission rate for patients treated in the ED with methylprednisolone versus placebo; however, this finding was not statistically significant in patients 24-54 months old.[16]

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For those requiring hospitalization, length of hospital stay and time until readiness to discharge were the primary outcomes assessed by Panickar et al. and Jartti et al. Neither study found a statistically significant difference between groups who received oral prednisolone versus placebo for 3 or 5 days. Secondary outcomes such as symptom scores, symptom duration, albuterol use, and 60-day relapse rate were also not improved in those taking oral prednisolone compared with placebo.[14,15]

The mixed results of studies assessing the efficacy of SCS in preschool-aged wheezing children may be attributed to the fact that wheezing in this age group likely represents multiple underlying processes. Most acute wheezing at this age is not associated with atopy and is often triggered by viral respiratory tract infections.[17] Furthermore, 90% of wheezing in children under the age of five years does not persist to the asthma phenotype (recurrent episodes with multiple triggers, airway obstruction, and hyper-responsiveness) once they reach school age.[18]

While SCS are generally not expensive, their use is not without cost. Studies of oral corticosteroid use in children with asthma have shown adverse effects including vomiting, hypertension, and impaired growth.[19] Children with recurrent wheeze receiving SCS may demonstrate biochemical hypothalamic-pituitary-axis dysfunction.[20] Given the high utilization and SCS prescription rates in this age group, reducing the use of SCS with wheezing episodes could have a large clinical and financial impact.[3,4] These medications should be used judiciously in order to balance benefit with potential risks.

WHEN MIGHT SYSTEMIC CORTICOSTEROIDS BE HELPFUL IN WHEEZING PRESCHOOLERS

Given that there is diversity in the phenotype of preschool-aged children who wheeze, it is possible that a subset of these children would benefit from SCS. Some studies have shown that certain groups of patients derive benefit, including those with rhinovirus infection, eczema, and children at higher risk for multitrigger asthma.[11,13] Children who have atopic wheeze are more likely to have persistent symptoms that may eventually be diagnosed as asthma.[18] These children will have airway inflammation secondary to eosinophilic infiltration and may be responsive to SCS at times of exacerbation. However, attempts to classify preschool children based on risk of asthma have not shown consistent results.

The Asthma Predictive Index (API), a tool developed as a part of the Tucson Children's Respiratory Study, uses clinical factors including history of wheeze, atopic dermatitis, and allergic rhinitis to determine a young child's risk of having asthma symptoms after age six years.[21] Jartti et al. and Panickar et al. used the API to stratify patients based on future asthma risk.[13,15] The high risk group in the Jartti et al. study showed the benefit of SCS, while there was no benefit in the Panickar et al. study. When Oommen et al. also attempted to stratify asthma risk using levels of blood eosinophil proteins, which when elevated, are predictive of persistent wheeze.[14] There was no difference in drug efficacy between patients with high and low blood eosinophil proteins. Although Foster et al. demonstrated shorter length of stay (LOS) with SCS overall, this was only seen in the subgroup with a previous diagnosis of asthma.

Patients presenting with severe disease (including those requiring critical care or with the highest symptom scores) have mostly been excluded from these studies. Although patients with severe disease often receive steroids, there is insufficient evidence of the efficacy of SCS in this population.[12,13,15,22] Foster et al. did include patients with high symptom scores (although they excluded patients with "critical wheeze") and found that the efficacy of SCS was clearest for those with severe presentations.[11]

Finally, some studies have demonstrated a virus-specific effect, with a reduction in time to readiness for discharge and reduction in recurrent wheeze in children treated with prednisolone who were positive for rhinovirus.[12,23] Rhinovirus infection has also been associated with allergic sensitization and recurrent wheezing.[23,24] However, rhinovirus-specific steroid responsiveness has not been consistently replicated by other investigators.[11]

WHAT YOU SHOULD DO INSTEAD

The majority of preschool-aged children presenting with wheeze in the care of hospitalists have mild to moderate symptoms, triggered by viral infections.[22] It can be helpful to categorize the wheezing child as atopic or nonatopic. Laboratory studies such as allergen-specific IgE, peripheral eosinophil count, and exhaled nitric oxide can aid in predicting response to asthma medications and progression to the classic asthma phenotype.[25] In the absence of these diagnostic studies, which are often costly and challenging to obtain in young children, a clinical score such as the API, or the recently validated Pediatric Asthma Risk Score (PARS), can help to assess future risk of developing multitrigger asthma.[21,26] A positive API requires a history of more than three episodes of wheeze over the past year as well as one major (physician-diagnosed atopic dermatitis or parental asthma) or two minor (peripheral blood eosinophilia, physician-diagnosed allergic rhinitis, or wheezing apart from colds) criteria.[17] It has a sensitivity of 57% and specificity of 81%.[26] The PARS uses the presence of parental asthma, eczema, early wheezing, wheezing apart from colds, African-American race, and ≥2 positive skin prick tests to predict asthma. The sensitivity and specificity of PARS are similar to the API at 68% and 79%, respectively.[26]

Given the mixed results from studies evaluating the benefit of SCS in preschoolers with atopic symptoms and/or a positive API, evidence is lacking to guide decision-making in these children.[13-15] However, it is reasonable to treat those at higher risk for future multitrigger asthma with SCS. There is also insufficient evidence to determine whether those with more severe disease or those infected with particular viral pathogens may benefit. Therefore, for the majority of children presenting with viral-induced wheezing, with a negative API or low PARS, there is no evidence that treatment with an SCS provides benefit in the form of reduced LOS, reduction in clinical symptoms, treatment failure, or relapse rate.

RECOMMENDATIONS

- Do not routinely treat with SCS preschool-aged children who have episodic wheezing triggered by viral respiratory

tract infections and who do not have risk factors for persistent asthma.
- For preschool-aged children with a history of atopy, a positive API, or elevated PARS, SCS can be considered during admissions for respiratory distress and wheezing.
- Preschool-aged children presenting with severe disease or requiring intensive care may benefit from SCS, but there is insufficient evidence to conclude whether this practice provides benefit.

CONCLUSIONS

Current evidence does not support the routine use of SCS for preschool-aged children admitted for mild to moderate wheezing episodes. The majority of these children have viral episodic wheeze that does not develop into the asthma phenotype. For children with severe disease or at higher risk for asthma, SCS may be considered, although there remains insufficient evidence as to their efficacy. The patient in the introductory case lacks risk factors that would suggest SCS responsiveness (eg, positive API, previous asthma diagnosis, inhaled corticosteroid use, or severe disease) and would likely receive no clinical benefit from dexamethasone treatment.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason?" Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason" topics by emailing TWDFNR@hospitalmedicine.org.

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