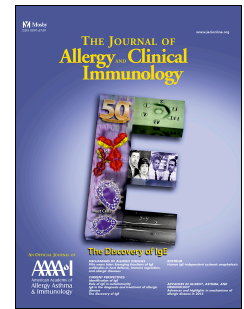


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Oral corticosteroids in preschool children with severe episodes of virus-associated wheeze: to treat or not to treat?

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Clinical Preview

Oral corticosteroids in preschool children with severe episodes of virus-associated wheeze: to treat or not to treat?

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Acute episodic wheeze is a common clinical scenario during the preschool years, usually related to an infectious process. Traditionally, more severe episodes have been treated with oral corticosteroids (OCS), largely based on their demonstrated efficacy in acute asthma exacerbations among older children and adults. Despite their widespread use, most clinical trials that investigated OCS efficacy for acute episodic viral wheeze in the preschool population have failed to detect consistent beneficial effects¹. The exact explanation for this difference in response between preschool children and older children remains uncertain, but may be related to different patterns baseline of airway inflammation (i.e., neutrophilic vs. eosinophilic inflammation) which have differential susceptibilities to corticosteroid effects².

In the February 2018 issue of *Lancet Respiratory Medicine*, Foster and colleagues present the results of a randomized, double blind, placebo controlled, clinical trial, performed in Australia, investigating the utility of a 3 day course of oral prednisolone (1 mg/kg/day) compared to placebo among preschool children presenting for emergency department care with acute viral-associated wheeze³. The overall conclusion was that children treated with prednisolone experienced significantly shorter durations of hospital stay until they were ready for discharge.

Eligible patients were children aged 24–72 months presenting to the pediatric emergency department with a clinical diagnosis of wheeze and symptoms or signs of a viral upper respiratory tract infection. Exclusion of children below 24 months of age appropriately precluded the participation of children with viral bronchiolitis, a clinical syndrome unresponsive to systemic corticosteroids. Children with other significant medical history or prematurity (<34 weeks gestational age) were excluded. After assessing 3727 patients for eligibility, 624 were randomized, and 605 patients were included in the modified intention-to-treat analysis that was sequentially designed to first examine the hypothesis that placebo was non-inferior to prednisolone. Once this hypothesis was rejected (i.e., placebo was indeed inferior to prednisolone in term of length of stay), a *post hoc* superiority analysis confirmed the hypothesis

that prednisolone was superior to placebo. The median length of stay until ready for discharge was significantly longer in the placebo group (540 min [IQR 124–971]) compared to the prednisolone group (370 min [IQR 121–709]); unadjusted ratio of the length of stay was 0.79 (95% CI; 0.64–0.97; $p=0.0227$). The difference between the groups remained significant after adjustment for age, personal or family history of atopy, baseline severity score, and presence of respiratory virus antigen in upper airway sample. Predictors for a favorable OCS response included features of severe wheeze at presentation (pulmonary score >5 on a scale of 0-9), receiving salbutamol prior to the ED visit, and prior diagnosis of asthma. The presence or the type of respiratory virus detected was not related to OCS response. The rate of adverse events was comparable between the groups, and 5% of patients received open-label prednisolone during the hospital stay after receiving the first dose of study medication. Unfortunately, no data are presented about rates of symptom relapse and return to the ED within 7 days following study participation, but over the 3 months following discharge, comparable numbers of children in both groups required subsequent ED care.

The results of this trial should be viewed in the broader context of 5 previous clinical trials examining the utility of OCS for acute episodic wheeze¹. Two clinical trials performed in the outpatient setting were negative¹. More relevant is the trial by Panickar *et al*⁴, the only randomized trial that investigated OCS efficacy in the inpatient setting. In that trial, 700 children aged 10-60 months were randomized to receive oral prednisolone or placebo for 5 days. Neither the duration of hospitalization, the primary outcome, nor any of the secondary outcomes, differed between the groups. The reason(s) for the differences in outcomes between this trial and that reported by Panickar are uncertain. These may be related to differences in the severity of the episodes, as suggested by greater effect of OCS in the Foster trial³ among children with more severe episodes, who have greater opportunity to improve with a given intervention than those with milder episodes. Additionally, the exclusion of children younger than 2 years in the Foster trial³ likely enriched the study population with children with diagnosed asthma or at greater likelihood to become asthmatic, and this is supported by greater OCS response among those children with a pre-existing asthma diagnosis.

Do the results of this clinical trial advance our understanding of this ongoing clinical dilemma in terms of what role OCS play in the management of episodic viral-associated wheeze? Based on the currently available trials, there is no evidence that OCS is an effective therapy for acute episodic viral wheeze among preschool children who are managed at home. However, these new data by Foster *et al* support the long-standing practice that preschool children with acute episodic viral-associated wheeze requiring emergency department care, particularly children with a diagnosis of asthma, receipt of bronchodilators prior to ED arrival, or more severe wheezing episodes, be treated with OCS in order to reduce the duration of hospital-based care. Additional studies are still needed to best determine which subgroups of children receive greatest benefit from this approach.

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