

Should we give steroids to all preschool aged children with viral-induced wheezing?

Panickar et al. Oral prednisolone for preschool children with acute virus-induced wheezing. N Engl J Med 2009;360:329-38.

Take Home Message: A 5-day course of oral prednisolone for preschool children with viral-induced wheezing did not significantly shorten duration of hospital or severity of symptoms as compared to placebo.

Highlights: There has been conflicting evidence regarding the efficacy of corticosteroids for preschool children with viral-induced wheezing. Panickar et al. performed a double-blind, placebo-controlled trial^[1], randomizing children with viral-induced wheezing to either 5 days of prednisolone or placebo. They found no significant reduction in the duration of hospital stay, their primary outcome, or in doctor and parent assessed respiratory scores, or hospital readmission within 1 month. They comment that a possible explanation for their negative result as compared to other studies is that the majority of the children in the trial did not have a classic atopic asthma phenotype. However, they did perform a subgroup analysis looking at children who were at high risk for asthma at school age and also found no significant differences in the prednisolone group.

The Nitty-Gritty:

Design:

- o Randomized, double-blind, placebo-controlled trial
- o N= 687

§ Prednisolone group (n= 343)

§ Placebo group (n=344)

o Setting: Three hospitals in the United Kingdom

o Enrollment: 2005-2007

o Primary outcome: duration of hospitalization

o Analysis: Intention-to-treat

Population:

o **Inclusion Criteria:** Children aged 10 months-60 months who had an attack of wheezing judged clinically to be preceded by a viral upper respiratory tract infection

o **Exclusion Criteria**

§ Children in shock

§ Clinical evidence of bacterial sepsis

§ Known heart or lung disease

§ Receiving immunosuppressive therapy or known immunodeficiency

§ Active varicella infection, or recent exposure to varicella

o **Baseline Characteristics** – from the prednisolone group, no significant differences between the two groups

§ **Male sex:** 66.2%

§ **Age:** 25.8±13.3 months

§ **Previous wheezing:** 63.6%

§ **Age at first onset of wheezing:** 16.6±12.0 months

§ **Coughing or wheezing without a cold during previous year:** 14.2%

§ **Previously diagnosed asthma:** 18.9%

§ **Previously diagnosed eczema:** 41.2%

§ **Previously diagnosed hay fever:** 8.0%

§ **Previously diagnosed food allergy:** 10.1%

§ **Previously diagnosed bronchiolitis:** 22.0%

§ **Family history of asthma in mother:** 26.6%

§ **Family history of asthma in father:** 25.5%

§ **Smokers in household:** 35.3%

§ **No. of wheezing attacks in previous year:**

- 0: 38.6%
- 1-3: 31.6%
- 4-6: 18.8%
- 6-10: 7.0%
- >10: 4.0%

§ **No. of previous presentations to hospital with acute wheezing:**

- 0: 78.8%
- 1-2: 14.8%
- 3-4: 3.9%
- ≥ 5 : 2.4%

§ **Parent-reported fever associated with symptoms: 30.7%**

§ **Previously prescribed medications:**

- **Inhaled albuterol as required: 50.6%**
- **Daily inhaled corticosteroids: 17.9%**

- **Oral montelukast:** 0.6%

§ **No. of course of oral corticosteroids for wheezing in the past year:**

- 0: 73.3%
- 1-2: 19.1%
- 3-4: 4.2%
- ≥ 5 : 3.3%

§ **Baseline Preschool Respiratory Assessment Measure (PRAM) score** (ranges from 0-12, with higher scores indicating a greter severity of respiratory distress):
4.32 \pm 2.31

· **Intervention:**

- o Randomized to either prednisolone (10 mg for children ≤ 24 months, or 20 mg for children > 24 months) once a day for 5 days or to placebo
- o All children were treated with albuterol initially and then subsequently as deemed necessary by providers
- o Time of decision to discharge and actual discharge were recorded

o Preschool Respiratory Assessment Measure (PRAM) scores, a validated respiratory score, were recorded at 4 hours, 12 and 24 hours and then parents were provided with a diary card for reporting respiratory symptoms at home after discharge

· **Outcomes:** comparisons are prednisolone group vs. placebo group

o **Primary outcome:**

§ **Median time to discharge:** 11.0 hours vs. 13.9 hours (ratio of geometric means, 0.90; 95%CI 0.77-1.5, P=0.18)

o **Secondary outcomes:**

§ **Total metered-dose inhaler actuations of albuterol (no.):** 52.80±74.50 vs. 66.70±88.10 (difference -14.08, 95%CI -26.62 to 1.54)

§ **PRAM score:**

· **At 4 hours:** 2.48±2.20 vs. 2.75±2.30 (difference -0.29, 95%CI -0.65 to 0.06)

· **At 12 hours:** 2.59±1.98 vs. 2.28±2.03 (difference 0.20, 95%CI -0.24 to 0.64)

· **At 24 hours:** 1.52±1.75 vs. 1.52±1.64 (difference -0.06, 95%CI -0.57 - 0.51)

§ **Substitution of a study drug and introduction of definitive system corticosteroid:** 4.5% vs. 6.2% (OR 0.70, 95% CI, 0.34 to 1.46)

§ **Respiratory symptom score at 7 days** (assigned by parents provided with a symptom diary card): 1.00 ± 0.69 vs. 1.10 ± 0.65 (difference -0.06, 95%CI, -0.18 to 0.07)

§ **Actuations of albuterol at 7 days:** 10.60 ± 8.30 vs. 10.80 ± 9.50 (difference -0.24, 95%CI -1.95 to 1.45)

§ **Time to return to normal activities (days):** 5.13 ± 3.90 vs. 5.10 ± 3.84 (difference 0.06, 95% CI -0.59 to 0.67)

§ **Hospital readmission for wheezing within 1 month after discharge:** 7.4% vs. 6.3% (OR 1.19, 95%CI, 0.62 to 2.26)

- **Subgroup Analysis:** children classified at being high risk for asthma at school age – no significant difference between the placebo group and the prednisolone group in duration of hospitalization, and no evidence of a differential treatment effect, as compared with children who were not in the high-risk group

- **Adverse Events:** none

- **Criticisms**

- o Comparing duration of hospitalization between two groups as geometric means after data underwent logarithmic transformation does not reveal the presence of outliers and can potentially mask differences between the groups^{[\[ii\]](#)}

- o Such rapid improvement in the placebo group may obscure any treatment effect^{[\[iii\]](#)}

- o Inclusion of first-time wheezers who may have minimal responsiveness to corticosteroids may have confounded the results^{[\[iv\]](#)}

o Corticosteroids may not be indicated in children with mild asthma which many of the children seemed to have based on their PRAM scores iv

o No PRAM score was obtained before the first dose of albuterol.[v]

[i] Panickar et al. Oral prednisolone for preschool children with acute virus-induced wheezing. *N Engl J Med* 2009;360:329-38.

[ii] Koumbourlis AC. Oral corticosteroids in children with wheezing. *N Engl J Med* 2009; 360:1673.

[iii] Weinberger M. Oral corticosteroids in children with wheezing. *N Engl J Med* 2009; 360: 1673-4.

[iv] Ducharme et al. Oral corticosteroids in children with wheezing. *N Engl J Med* 2009; 360: 1674.

[v] Mroueh S. Oral corticosteroids in children with wheezing. *N Engl J Med* 2009; 360: 1675.