Does Treatment with Inhaled Corticosteroids Improve Outcomes in Infants with RSV Infection?

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Question: Does treatment with inhaled corticosteroids improve outcomes (oxygen saturations, length of stay, mortality) in infants with RSV infection?

Answer: Most likely, no.

Date Answer Determined: December 23, 2006

Level of Evidence for the Answer: B

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A Summary of the Issues

Bronchiolitis, including cases caused by Respiratory Syncytial Virus, is the most common lower respiratory tract infection in infancy. This infection can lead to extensive morbidity including hypoxemia, hospitalization, and even death. The main principle of therapy has been supportive, with bronchodilators and supplemental oxygen used to help relieve wheezing and hypoxemia. Pharmacologically corticosteroids inhibit recruitment of neutrophils, monocytes, and macrophages into areas of inflammation. Inhaled steroids offer the benefit of decreasing systemic absorption, causing fewer systemic side effects.

Summary of the Evidence

Wong, et al conducted a single-center double-blind randomized placebo-controlled trial from March 1994 to April 1996 [1]. In this study 48 previously healthy infants, two weeks to 12 months of age, diagnosed with RSV bronchiolitis, were randomized to treatment and control groups. The age range of the infants was 2 weeks of life to 12 months of life. The treatment arm received 150 micrograms of fluticasone propionate twice daily for three months via a Babyhaler MDI and spacer. The control group received a placebo inhaler. Longitudinal assessments were obtained seven times over the following year. Lung function studies were measured at 6 month post discharge. Health records, clinical exams, overnight cough recordings, and oxygen saturations were also measured. Completing the trial were 21 infants from the treatment arm and 22 infants from the placebo arm. In regard to oxygen saturations, the baseline median (range) values were 95% (91-98%) for the treatment group and 96% (90-97%) for the placebo group. There was no statistical difference in median saturation values during the early weeks of therapy or anytime thereafter. Oxygen levels below 94% and 90% occurred at the same rate. There was also no statistical difference in hospital-stay days with a mean of 3.2 days for the inhaled steroid treatment arm and 3.5 for the placebo treated study arm.

Richter and Seddon conducted a randomized, double-blind, placebo-controlled trial that included 40 infants with RSV bronchiolitis [2]. The mean age of the infants was 13.5 weeks (range: 4 to 41 weeks). Twenty-one infants randomized to the treatment arm received one milligram of nebulized budesonide every 12 hours for five days, followed by 500 micrograms nebulized every 12 hours for a total of six weeks. Nineteen infants randomized to the placebo arm received nebulized normal saline twice daily for six weeks. There was no statistically significant difference between the two groups regarding either mean oxygen requirements or length of hospital stay.

Bentur, et al conducted a double-blind, placebo-controlled randomized controlled trial [3]. The treatment arm was with 0.25 milligrams of nebulized dexamethasone every six hours. The placebo group received nebulized 0.9% normal saline. Sixty-one infants with RSV brochiolitis were randomized at time of hospital admission. The range of patient age was 3 to 12 months. All study participants received epinephrine nebulizations as part of their treatment protocol. Results failed to show a clinically significant difference in oxygen saturation scores between the two groups. Data examination using the Kaplan-Meyer method did show a statistically significant difference in hospitalization rates at days five and six of hospitalization ($p<0.038$). Further sub-set analysis showed a statistically significant difference in length of stay for children that were born prematurely. For the treatment group the hospital length of stay was (6.5 +/- 1.7 days) compared to placebo values of (9.1 +/- 1.9 days) ($p<0.018$).

Conclusions

A majority of studies failed to demonstrate a statistically significant improvement with inhaled steroids in regards to oxygen saturations or length of hospital stay. No study demonstrated improved oxygen

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saturation with inhaled steroids. One study did demonstrate a decreased hospitalization rate after five days of treatment. Further analysis showed this association was stronger in infants who were born prematurely. Overall, the results do not support the routine use of inhaled steroids in RSV bronchiolitis in children under one year of age.

Search Terms

Inhaled corticosteroids, RSV, brochiolitis, length of stay, oxygen saturation, randomized controlled trial.

Inclusion criteria:

English language, randomized controlled trials that evaluated inhaled steroids in infant one year old or less. Those studies that included children over one year old, included systemic steroids, or did not evaluate oxygen saturation or length of hospital stay were excluded.

List of Articles Reviewed

1. Wong JY, Moon S, Beardsmore C, O'Callaghan C, Simpson H. No objective benefit from steroids inhaled via a spacer in infants recovering from bronchiolitis. *European Respiratory Journal.* 2000; 15(2): 388-394.
2. Richter H, Seddon P. Early nebulized budesonide in the treatment of bronchiolitis and the prevention of postbronchiolitis wheezing. *Journal of Pediatrics.* 1998; 132(5): 849-853.
3. Bentur L, Shoseyov D, Feigenbaum D, Gorichovsky Y, Bibi H. Dexamethasone inhalations in RSV bronchiolitis: a double-blind, placebo-controlled study. *Acta Paediatrica.* 2005; 94 (7): 866-71.