Bronchiolitis Burden Reduced by Combo Tx

BY MARY ANN MOON

The combination of oral dexamethasone and nebulized epinephrine appeared to reduce hospital admission, hasten discharge from the emergency department, and decrease the duration of symptoms in infants with bronchiolitis.

The researchers compared each of the drugs alone and in combination against placebo in a study of 800 infants aged 6 weeks to 1 year who presented to the ED with a first episode of bronchiolitis and signs of upper respiratory infection.

Hospitalizations for the disorder have almost doubled over the past 10-15 years in the United States and Canada, and treatment is controversial. "Bronchodilators and corticosteroids are widely used but not routinely recommended," said Dr. Amy C. Plint of Children's Hospital of Eastern Ontario, Ottawa, and her associates.

They conducted a randomized, double-blind, clinical trial at eight Canadian pediatric emergency departments. The patients had scores of 4-15 on the respiratory distress assessment index.

The primary outcome—hospital admission within 7 days of the ED visit—occurred in only 17% of the infants who received combined dexamethasone and epinephrine, compared with 24% of those who received epinephrine only, 26% of those who received dexamethasone only, and 26% of those who received placebo only. That represents a relative risk reduction of 35% with the combined therapy, the investigators said (N. Engl. J. Med. 2009;360:2079-89).

The benefit of dexamethasone plus epinephrine was evident within 3 days of presentation, and it was not affected by the duration or severity of the illness, whether the patient proved to have respiratory syncytial virus, or whether the patient had a history of atopy.

"We also found an apparent benefit from the combined therapy on our secondary outcomes: Infants in this group were discharged earlier from medical care and resumed quiet breathing and normal feeding sooner than did those in the placebo group," Dr. Plint and her colleagues said. "In contrast, neither dexamethasone alone nor epinephrine alone had any effect on these outcomes."

There were no serious short-term adverse events related to treatment. However, "we do not have findings from long-term follow-up to establish whether our study treatments caused adrenal suppression, arrest of somatic growth, or neurodevelopmental delay," as has been suggested by some researchers.

"Given the unexpected synergy we found between epinephrine and dexamethasone, and the lack of any apparent benefit when either drug is used alone, our results should be considered exploratory," Dr. Plint and her associates noted. "Confirmation of our findings by a study powered specifically to compare combined epinephrine and dexamethasone therapy with placebo is needed."

In an editorial comment accompanying the report, Dr. Urs Frey of the University Hospital of Bern (Switzerland) and Dr. Erika von Mutius of University Children's Hospital, Munich, said that the effect size of the treatment benefit was small.

"Given [that] 11 infants would have to be treated to prevent one hospital admission, it does not seem practical to apply [this] treatment, especially considering the potential effects of high-dose corticosteroids on brain and lung development in such young children," they noted (N. Engl. J. Med. 2009;360:2130-1).

Instead, "it is essential during the first episode [of bronchiolitis in a preschooler] to provide supportive care—including supplemental oxygen, hydration, nutrition, and short-term bronchodilation—[but] the key intervention is close follow-up," they said.

Dr. Frey reported receiving a travel grant from GlaxoSmithKline PLC and research support from VoluSense AS. Dr. von Mutius reported receiving consulting fees from GlaxoSmithKline, UCB SA, and ProtectImmun GmbH, lecture fees from Novartis and Alk-Scherax-Abelló Arzneimittel GmbH, and grant support from Airsonett AB. Dr. von Mutius also was named as an inventor on a pending patent for protection from allergies and inflammatory disorders. ■