KiDrug Alert Journal Club

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A Critical Review of: "A randomized trial of nebulized 3% hypertonic saline with epinephrine in the treatment of acute bronchiolitis in the emergency department."

Grewal S, Ali S, McConnell DW, Vandermeer B, Klassen TP
Arch Pediatr Adolesc Med 2009 Nov; 163(11) 1007-1012

SUMMARY OF FINDINGS

Physicians continue to look for an effective treatment to alleviate respiratory distress in infants with acute bronchiolitis. Researchers in Edmonton, Alberta examined the effectiveness of nebulized 3% hypertonic saline with epinephrine compared with nebulized normal saline and epinephrine to improve respiratory distress in the emergency department as measured by the Respiratory Assessment Change Score (RACS) from baseline to 120 minutes. Forty-eight infants 6 weeks to 12 months with a diagnosis of mild to moderate bronchiolitis and oxygen saturations between 85%-96% were enrolled in the study. Patients were excluded if they had any pre-existing cardiac or pulmonary disease including asthma, previous bronchodilator use or severe illness requiring resuscitation.

Patients were randomized to receive 0.5ml of 2.25% racemic epinephrine with either 2.5ml of 3% hypertonic saline or 0.9% normal saline. Respiratory rate, oxygen saturation, heart rate and Respiratory Distress Assessment Instrument (RDAI) score were obtained at baseline and every 30 minutes for a total of 120 minutes. Physicians were able to order a second dose of the study medication at their discretion as well as prescribe any additional interventions. No statistically significant difference was noted in the change in RACS and oxygen saturation between the two groups at 120 minutes. The hypertonic saline group had 5 fewer hospital admissions, an absolute difference in admission rate of 22%; however, this did not reach statistical significance.

COMMENTS

Acute bronchiolitis is the most common lower respiratory infection in infants. It accounts for 90,000 hospitalization annually at a cost of $700 million in the United States.[1] Unfortunately, there are few effective treatments, particularly for use in the emergency department and outpatient setting. Bronchodilators and corticosteroids have not been shown to improve clinical scores or decrease hospital admission rates.[2,3] Given the large burden on the health care system it is imperative that an effective treatment for bronchiolitis is found that improves clinical severity and/or decreases hospital admissions. Previous trials and a meta-analysis have demonstrated a potential role for nebulized hypertonic saline in improving clinical scores and the duration of hospital admissions.[3,4,5]

The study by Grewal *et al.* examines the effect of hypertonic saline in the emergency department on RACS 2 hours post treatment. Since publication of this study, there have been 2 studies evaluating the role of nebulized 3% hypertonic saline in the treatment of acute bronchiolitis in the ambulatory setting. Kuzik *et al*. examined whether 3 back to back masks of salbutamol with 3% hypertonic saline

compared to salbutamol with 0.9% normal saline reduced hospital admissions.[6] Like Grewal *et al*. they found no significant difference in RACS or rate of hospital admissions, however the study was underpowered. In the study by Al-Ansari *et al*, patients received either 5% or 3% hypertonic saline or 0.9% normal saline with epinephrine every 4 hours.[7] A statistically significant improvement in disease severity was seen at 48 hours, however, like the previously mentioned studies, no statistical difference was seen at 2 hours.

Grewal *et al*. did not find a statistically significant benefit with nebulized 3% hypertonic saline as compared with 0.9 % normal saline when administered with racemic epinephrine to improve respiratory distress. The clinically important question is, "does hypertonic saline reduce hospital admissions?". This and other studies have been underpowered to evaluate this outcome. The lack of benefit seen in this study may due to confounding because of the concomitant use of racemic epinephrine, a bronchodilator, the large percentage (70%) of patients enrolled with a family history of asthma and perhaps sample size. The hospital admission rate, 45% is also higher than in other reported studies[3-4,6,8], and may represent inclusion of a more severe population than the intended mild to moderate disease or a lower threshold for admission. Given the safety profile of hypertonic saline and trials demonstrating an improvement in clinical scores and duration of hospital admissions, a large study examining nebulized 3% hypertonic saline versus saline without bronchodilators should be conducted.[3,4]

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