

Worksheet for Using an Article About Therapy or Prevention

Journal Club Eastern Virginia Medical School

Valerie Baur 1/26/09

CITATION: Kuzik BA, Al Qadhi SA, Kent S, Flavin MP, Hopman W, Hotte S, et al. Nebulized hypertonic saline in the treatment of viral bronchiolitis in infants. *Journal of Pediatrics* 2007; 151: 266-70

I. WHAT IS BEING STUDIED?	
1. Study Objective	To investigate the use of nebulized 3% hypertonic saline for treating bronchiolitis in moderately ill hospitalized infants by prospective, randomized, double-blinded controlled multi-center trial.
2. Study Design	96 infants admitted to 3 regional pediatric centers during 3 consecutive bronchiolitis seasons 12/03-5/06. Randomized to receive repeated doses of either nebulized 3% HS or 0.9% NS in addition to “routine therapy” prescribed by an attending physician.
3. Inclusion Criteria	Infants up to 18 mo. Admitted for moderate to severe viral bronchiolitis. With symptoms of preceding URI, wheeze or crackles, PLUS desats below 94% on RA or Respiratory distress by RDAI > 4.
4. Exclusion Criteria	H/o previous wheezing, chronic cardiopulm disease, chronic immunodeficiency, critical illness necessitating ICU admission, prematurity below 34 wks, or h/o receiving neb HS with 12 hrs
5. Interventions Compared	Nebulized NS 0.9% vs. Neb HS 3% Q2h x 3 doses, Q4h x 5 doses, Q6h until discharge.
6. Outcomes Evaluated	Primary outcome= LOS Discharge criteria: RDAI <4 and SaO2 >94% on RA for at least 4 hours(55%), OR discharge by attending physician (45%)
II. Are the results of the study valid?	
1. Was the assignment of patients randomized?	Yes, Randomized by computer.
2. Were all patients who entered the trial	Yes. 96 enrolled. 5 withdrawn (3 from NS)

properly accounted for and attributed at its conclusions?	group, 2 from HS group) at parental request, but included in intention-to-treat analysis
3. Was follow-up complete?	Yes, patients only followed to discharge.
4. Were patients, health workers and study personnel “blind” to treatment?	Yes, preparation of NS and HS were prepared by research pharmacist, all participants were blinded.
5. Were study groups similar at the start of the trial?	Yes, similar time of presentation, both groups presented with borderline hypoxia, moderate respiratory distress. 69% RSV positive.
6. Aside from the experimental intervention, were the groups treated equally	Study alleges that “add on” treatments were comparable between groups. These included albuterol, racemic epinephrine, antibiotics, and steroids, in addition to the study solutions. Although these additional treatments may cloud the results, there was no significant difference between study groups.
III. What were the results?	
1. How large was the treatment effect? (difference between treatment and control group).	26% reduction in LOS for HS group. =average decrease in LOS by approx 1 day. (3.5 +/- 2.9 days vs. 2.6 +/- 1.9 days)
2. What was the estimated treatment effect at a 95% confidence interval?	Reduction in LOS by approx 1 day. However,
IV. Will the results help me in caring for my patients? (applicable ?)	
1. Were all clinically important outcomes considered?	No. LOS for admitted patients may not be particularly applicable to emergency medicine. Did not study effect of HS on acute Resp distress/hypoxia in bronchiolitis.
2. Are treatment outcomes worth the potential harms?	No participants were withdrawn by medical staff. No documented adverse effects of HS. However, it can be associated with bronchoconstriction in asthmatics. This potential effect can be mitigated by co-

	administration of bronchodilators. Advantages appear to outweigh small potential risks.
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Additional Comments:

The major drawback of this study is its small sample size. Although the difference in LOS between treatment and control groups was significant ($p=.05$), the confidence intervals overlap (3.5 +/- 2.9 days for NS vs. 2.6 +/- 1.9 days for HS). This suggests that larger studies are indicated and that perhaps the study was under-powered.

Some may argue that since the study only involved admitted patients, it is not relevant to the practice of emergency medicine. However, if HS is proven to be beneficial in acute viral bronchiolitis, earlier administration while patients are still in the ED may increase the response to treatment. This could be an area of further study in this area as well.

Finally, editorial comments on this study have suggested that it is invalidated by the inclusion of “additional therapy” prescribed by the attending physician. However, the study carefully documents all such additional treatments and shows no difference between the control group and the treatment group in regard to these add-on treatments. (See Table III.) Since new treatments are usually compared to “standard therapy” plus or minus a placebo like the one found in this study, including add-on treatments does not invalidate this study.

CLINICAL BOTTOM LINE:

In children under 18 months with acute viral bronchiolitis, nebulized 3% hypertonic saline has a low risk of adverse effects and may hasten recovery and lead to earlier discharge among admitted patients when compared to standard therapy alone. However, there is no evidence to suggest that use of HS in the ED will decrease rates of hospital admission and further studies are required to quantify the potential benefits of this intervention.

Additional References:

Calogero C, Sly PD. Acute Viral Bronchiolitis: To treat or not to treat- that is the question. *The Journal of Pediatric*; 2007: 235-7.