7% Hypertonic Saline in Acute Bronchiolitis: 
A Randomized Controlled Trial


SUMMARY
This randomized controlled trial compared 7% hypertonic saline versus 0.9% (normal) saline, in addition to racemic epinephrine (in both groups), among infants with mild to moderate severity bronchiolitis. The authors used a modification of the oft-applied bronchiolitis severity score (BSS) by Wang, et al. [1] to evaluate the efficacy of treatment at multiple time points until discharge/disposition from the hospital. They reported no statistically significant differences between the groups for changes in modified-BSS after 1 dose of treatment as well as until final disposition from the hospital.

COMMENTARIES
Evidence-based-medicine Viewpoint
This study has the usual methodological refinements associated with a high-quality trial, including appropriate sequence generation, block randomization, allocation concealment and double-blinding (especially the outcome assessor). Although a convenience sample was enrolled, the number included was pre-calculated and adequately powered. The cohort of infants was consistent with the usual clinical understanding of bronchiolitis. Clinically relevant outcomes were chosen for evaluation of efficacy.

Some years back, Indian Pediatrics explored the issue of hypertonic saline as an adjunct therapy in bronchiolitis [2], and concluded that there was insufficient robust evidence to include it in routine practice. However, a Cochrane systematic review [3] published around the same time suggested a beneficial effect of hypertonic saline in terms of statistically significant reduction in clinical severity score and duration of hospital stay. At that time, all available studies had compared 3% hypertonic saline against normal saline. There is a single recent trial that used 5% hypertonic saline in some patients [4] but results are presented together with those receiving 3% saline. In that sense, this trial by Jacobs, et al. evaluating 7% hypertonic saline is the first of its kind. In fact, the authors have used this to justify their trial, expecting that 7% saline would be even more beneficial than 3% saline.

It is therefore surprising that Jacobs, et al. failed to mention the updated version of the Cochrane review published in May 2013 [5] that included a total of 11 trials. This review corroborated the previous version, again showing a statistically significant reduction in severity score and hospital stay. Strictly speaking, the trial by Jacobs, et al. may not be comparable to the trials included in the Cochrane review, as the intervention and the measurement tool for outcomes were different. However, the benefit of alluding to it would have been to report the findings using the same tools for outcome measurement as all the previous trials. This would have made it possible to incorporate Jacobs’ findings into the meta-analysis and assess its impact on the results available thus far.

This trial suggests that 7% hypertonic saline added to epinephrine may not provide additional benefit in bronchiolitis, although the balance of evidence is leaning towards adding 3% hypertonic saline to epinephrine for infants with bronchiolitis. The implications for research are two-fold viz that additional randomized trials may be required to resolve the issue and more important – new research should be conducted with an attempt to enrich existing knowledge, rather than for the sake of research itself.

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Pediatric Pulmonologist’s Viewpoint
The debate on bronchiolitis and its management will remain a controversy for many years to come and the final word might be difficult to arrive at – with the present background. Bronchiolitis is defined as a clinical syndrome in children less than 2 years of age, characterized by upper respiratory tract symptoms followed by lower respiratory tract signs and symptoms – with no other explanation for the wheezing. However, the first episode of wheeze can be an overlap manifestation of episodic virus-induced wheezing or acute viral-triggered
asthma. It is pertinent to remember that all first episodes of wheeze in young children within the agreed clinical definition are only “probable bronchiolitis”.

Inhaled epinephrine for bronchiolitis was found to be of benefit in the first day of care [6]. Nebulized 3% saline significantly reduces clinical severity score and also the length of hospital stay among children with non-severe acute bronchiolitis [5]. However a recent randomized control study in Indian context failed to elicit a favorable response [7]. In Indian children with cystic fibrosis, 3% hypertonic saline nebulization was better than 7% saline inhalation as a mucolytic [8].

A major hurdle in an interventional study is the difficulty to differentiate bronchiolitis from virus-induced wheeze or asthma, as each category responds differently making it difficult to determine the effect of each medication. Further, presence of two drugs – that could have a synergistic or antagonistic effect – makes the assessment of the effect of a single drug in such combination difficult. The present study is thought-provoking by being the first study with 7% saline. In clinical practice, 3% saline would remain the preferred choice when warranted. The use of 7% saline as a concept is interesting, but for now – is not promising.

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REFERENCES