

# Hypertonic saline for bronchiolitis in infants

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## Abstract

**Question** Recently, a 1-year-old patient returned from admission in the hospital for bronchiolitis, and the report I received indicated that he was treated with inhaled hypertonic saline, among other treatments. Is this therapy recommended for children in the acute care setting?

**Answer** Bronchiolitis, caused mostly by respiratory syncytial virus, is very common in the winter. It is the most frequent cause of hospitalization in infancy. Several good studies have been conducted in the past decade on the use of nebulized hypertonic saline for bronchiolitis management; however, they offer conflicting results. While there might be a role for the use of nebulized hypertonic saline in children who are hospitalized with bronchiolitis for more than 3 days, treatment in other settings does not confer enough benefit to recommend its use.



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**B**ronchiolitis is the most common lower respiratory tract infection in infants and children younger than age 2 and it is the most frequent cause of hospitalization in infancy. The rate of hospital admission for bronchiolitis has increased substantially in North America over the past 2 decades; the hospital admission rate among Canadian children with bronchiolitis increased from 15 to 39 admissions per 1000 children per year.<sup>1</sup> Although several viruses can give a similar clinical picture of fever, cough, rhinorrhea, and a variable degree of respiratory distress, respiratory syncytial virus is the predominant pathogen responsible for acute bronchiolitis.<sup>2,3</sup> Despite decades of research, supportive care ensuring adequate hydration and oxygenation remains the cornerstone of therapy for these infants.<sup>4</sup>

## Hypertonic saline for bronchiolitis

Over the past 2 decades, research on bronchiolitis management has explored the use of nebulized hypertonic saline. Theoretical mechanisms of action for hypertonic saline include inducing an osmotic flow of water into the mucus layer, thus rehydrating the airway surface liquid and improving mucociliary clearance, as well as reducing airway edema by absorbing water from the mucosa and submucosa.<sup>5</sup>

The earliest study with hypertonic saline included 65 infants with mostly mild bronchiolitis seen in the ambulatory setting in Israel. In this study, 3% hypertonic saline with terbutaline inhalation, given 3 times a day for 5 days, improved clinical severity scores significantly

compared with normal saline with terbutaline ( $P < .005$ ). The authors noted that the same effect might not have been seen if the infants had had clinical scores representing more severe illness.<sup>6</sup>

## Hypertonic saline with epinephrine

The use of epinephrine in conditions affecting the respiratory system is supported by its ability to cause vasoconstriction (resulting in decongested mucosa), regulate pulmonary blood flow, relax bronchial muscles, suppress chemical mediators, and reduce edema and catarrhal secretions in the upper airways by way of its antihistamine effect.<sup>7</sup>

While results of using epinephrine alone in the acute care setting are yet to be determined, a meta-analysis and a Cochrane review suggest that epinephrine might have a positive effect on bronchiolitis in the outpatient setting when compared with salbutamol and placebo.<sup>8,9</sup>

Addition of epinephrine to saline inhalations leads to mixed results. In a Canadian study, nebulized 3% hypertonic saline mixed with racemic epinephrine was not better than nebulized normal saline mixed with racemic epinephrine in improving clinical outcomes in 46 children with bronchiolitis visiting an emergency department (ED). Illness severity resulted in an admission rate of 45% in this cohort. Mean change in the Respiratory Assessment Change Score (RACS), representing respiratory distress, and change in oxygen saturation were not statistically significant when the hypertonic group was compared with the control group. The admission rate

was 22% lower in the hypertonic saline group; however, this also was not statistically significant.<sup>10</sup>

In an Israeli double-blind randomized controlled trial, hypertonic saline with racemic epinephrine was better than nebulized normal saline with racemic epinephrine given 3 times a day until discharge for 52 nonasthmatic infants with bronchiolitis. Mean clinical severity scores were improved on the first, second, and third day (7.3%, 8.9%, and 10%, respectively;  $P < .001$ ), and hospital stay was decreased among those receiving 3% hypertonic saline solution by 25% compared with those receiving normal saline ( $P < .05$ ).<sup>11</sup>

The same group continued to recruit patients and the combined multi-season data suggested significant improvement in the group treated with 3% hypertonic saline. Mean (SD) clinical scores were 7 (1) in the hypertonic saline group and 6.25 (1.1) in the normal saline group ( $P < .05$ ) on day 1, and 6.45 (1) and 5.35 (1.35), respectively, on day 2 ( $P < .05$ ). Hospital stay was also significantly shorter ( $P < .05$ ).<sup>12</sup>

### Hypertonic saline with bronchodilators

Another double-blind randomized controlled Canadian study compared 3 consecutive doses of either nebulized 3% hypertonic saline and salbutamol or normal saline and salbutamol. A total of 81 children who presented to 4 general hospital EDs were included. While no statistically significant differences were found between the 2 groups, children in the hypertonic saline group had a trend toward greater improvement with a same-day admission rate of 18% (95% CI 9% to 32%) versus 27% (95% CI 16% to 42%). The RACS was lower in the hypertonic saline group than in the normal saline group; however, the differences were not statistically significant.<sup>13</sup>

### Recent studies

The most recent Cochrane review on bronchiolitis, published in 2013, examined the effects of nebulized hypertonic saline. This review, including 11 trials and more than 1000 children with mild to moderate bronchiolitis, suggested that treatment with nebulized 3% saline resulted in a significantly shorter length of hospital stay compared with nebulized normal saline (mean difference 1.15 days; 95% CI 1.49 to 0.82;  $P < .00001$ ), as well as a significantly lower clinical score (day 1,  $P = .0004$ ; day 2,  $P = .001$ ; day 3,  $P < .00001$ ).<sup>14</sup> The meta-analysis also revealed that no significant short-term effects of up to 3 doses of nebulized hypertonic saline were observed in ED patients; however, the pooled results of 4 ED trials did show a 37% reduction in the rate of hospitalization among those treated with nebulized 3% saline compared with those treated with normal saline (not statistically significant).<sup>14</sup>

In a UK multicentre, open, parallel-group randomized controlled trial with more than 300 infants with bronchiolitis requiring oxygen supplementation and

admission, there was no difference in being ready for discharge (hazard ratio 0.95, 95% CI 0.75 to 1.20) or time of actual discharge (hazard ratio 0.97, 95% CI 0.76 to 1.23) between those receiving standard care alone and those receiving nebulized 3% hypertonic saline administered every 6 hours.<sup>15</sup>

In the ED setting, a double-blind randomized clinical trial conducted over 3 consecutive bronchiolitis seasons included more than 400 infants of at least 34 weeks' gestation and up to 2 years of age. They were given 4 mL of 3% hypertonic saline or normal saline inhaled up to 3 times after pretreatment with nebulized albuterol. The admission rate in children receiving 3% hypertonic saline was lower at 29% compared with 43% in those receiving normal saline (adjusted odds ratio 0.49 [95% CI 0.28 to 0.86]). Mean length of stay in hospital also decreased with hypertonic saline, but it was not statistically significantly shorter than in the normal saline group.<sup>16</sup> A second ED study reported contradicting results. Sixty-two infants with respiratory distress after a trial of albuterol were randomized to receive a single dose of either nebulized 3% hypertonic saline or normal saline. The hypertonic saline group showed less improvement in the RACS score at 1 hour compared with the normal saline group.<sup>17</sup>

In order to interpret studies with conflicting findings, one has to consider the small sample sizes and that the optimal concentration, dosing frequency, and duration of therapy of hypertonic saline has not yet been determined. Best outcome measures for studies evaluating hypertonic saline are also yet unknown. Until these issues are resolved, published trials will likely offer differing results.<sup>18</sup>

### National guidelines

In 2014, both the American Academy of Pediatrics and the Canadian Paediatric Society published updated position statements on the diagnosis and management of bronchiolitis for children younger than age 2. Both clinical practice guidelines do not support the use of nebulized hypertonic saline in infants with bronchiolitis in the ED; however, they both state that 3% hypertonic saline might be helpful in the inpatient setting, as it potentially benefits those patients who have a longer length of stay (exceeding 3 days).<sup>3,19</sup>

### Conclusion

Despite the considerable number of recently published trials on hypertonic saline and bronchiolitis, the evidence remains equivocal, and it should not be used routinely. There might be a role for the use of hypertonic saline in children who are hospitalized with bronchiolitis for more than 3 days. Until larger randomized controlled trials are conducted and systematic reviews are updated, the mainstay of treatment of bronchiolitis should remain supportive care. 

## Competing interests

None declared

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