3% Hypertonic Saline Versus Normal Saline in Inpatient Bronchiolitis: A Randomized Controlled Trial

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abstract

BACKGROUND AND OBJECTIVES: Bronchiolitis, the most common reason for hospitalization in children younger than 1 year in the United States, has no proven therapies effective beyond supportive care. We aimed to investigate the effect of nebulized 3% hypertonic saline (HS) compared with nebulized normal saline (NS) on length of stay (LOS) in infants hospitalized with bronchiolitis.

METHODS: We conducted a prospective, randomized, double-blind, controlled trial in an urban tertiary care children's hospital in 227 infants younger than 12 months old admitted with a diagnosis of bronchiolitis (190 completed the study); 113 infants were randomized to HS (93 completed the study), and 114 to NS (97 completed the study). Subjects received 4 mL nebulized 3% HS or 4 mL 0.9% NS every 4 hours from enrollment until hospital discharge. The primary outcome was median LOS. Secondary outcomes were total adverse events, subdivided as clinical worsening and readmissions.

RESULTS: Patient characteristics were similar in groups. In intention-to-treat analysis, median LOS (interquartile range) of HS and NS groups was 2.1 (1.2–4.6) vs 2.1 days (1.2–3.8), respectively, $P = .73$. We confirmed findings with per-protocol analysis, HS and NS groups with 2.0 (1.3–3.3) and 2.0 days (1.2–3.0), respectively, $P = .96$. Seven-day readmission rate for HS and NS groups were 4.3% and 3.1%, respectively, $P = .77$. Clinical worsening events were similar between groups (9% vs 8%, $P = .97$).

CONCLUSIONS: Among infants admitted to the hospital with bronchiolitis, treatment with nebulized 3% HS compared with NS had no difference in LOS or 7-day readmission rates.

WHAT'S KNOWN ON THIS SUBJECT: Bronchiolitis, the most frequent reason for hospitalization for infants younger than 1 year of age, has no proven treatments beyond supportive care. Although early studies suggested a potential benefit from 3% hypertonic saline, more recent studies have conflicting results.

WHAT THIS STUDY ADDS: This prospective, randomized, double-blind, controlled trial in infants admitted with bronchiolitis (including patients with a history of previous wheeze) demonstrated no difference in length of stay between those who received hypertonic saline or normal saline without bronchodilators.

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Dr Silver conceptualized and designed the study, coordinated and supervised data collection, participated in acquisition, analysis, and interpretation of the data, and drafted the initial manuscript; Drs Esteban-Cruciani, Azzarone, Douglas, Lee, Liewehr, Nazif, and Rhim helped with design of the study and acquisition of data, and reviewed the manuscript critically; Dr Agalliu contributed to study design, analysis and interpretation of data, and critically reviewed the manuscript; Dr Villegas contributed to study conceptualization and design, and critically reviewed the manuscript; Dr Rinke was involved in the analysis and interpretation of the data, and drafting and revising the manuscript; Dr O'Connor conceptualized and designed the study, coordinated and supervised data collection, participated in acquisition, analysis, and interpretation of the data, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Bronchiolitis is the most frequent cause of hospital admission among infants in the United States.[1–3] Total inpatient charges exceed $1.7 billion annually and mean length of stay (LOS) is 2.4 days.[3] Treatment of this common and costly condition is mainly supportive, as previous studies suggest little benefit from bronchodilators,[4,5] antibiotics,[6] or steroids.[7,8] Some suggest nebulized 3% sodium chloride, hypertonic saline (HS), is helpful,[9–14] but results are contradictory.[15–17]

Initial studies using HS for infants hospitalized with bronchiolitis suggest decreased LOS and improved severity scores.[9–14] Those studies differed from this study by excluding infants with previous wheeze, administering study medications with bronchodilators, or study subjects having much longer mean LOS.[9,10,13,14] A 2013 Cochrane review of HS in bronchiolitis referencing the aforementioned studies suggested 3% HS given with bronchodilators may be considered a safe and effective treatment of infants with mild to moderate bronchiolitis.[18] Subsequent studies[15,17,19,20] suggest no benefit from HS for inpatients, despite concomitant use of bronchodilators in all but one,[19] which differed by being an open study. Results in Wu et al[15] may be limited to a subpopulation with a diminished response to HS, as the study began in the emergency department (ED), demonstrating decreased admission rate with HS. The American Academy of Pediatrics (AAP) bronchiolitis guidelines updated in 2014 highlight the inconsistent findings regarding the effect of HS on LOS but suggest HS may be useful in infants admitted with bronchiolitis, particularly those with LOS >3 days.[21] It is imperative to investigate the true efficacy and safety of HS without confounding from bronchodilators, as unnecessary treatment can increase the financial burden of already costly bronchiolitis hospitalizations.

To understand the effects of HS in bronchiolitis, we conducted a randomized controlled trial to test the hypothesis that HS would decrease LOS in infants admitted with bronchiolitis without concomitant bronchodilators, including patients with previous wheeze.

METHODS

Study Design

We conducted a prospective, randomized, double-blind, controlled parallel-group study of infants admitted with bronchiolitis, comparing 3% HS with 0.9% normal saline (NS) from November 2011 through June 2014. The setting was an urban, tertiary care children's hospital with 136 beds, >8800 total admissions per year, and ~400 infants with bronchiolitis annually.

The principal investigator educated all physicians regarding the 2006 AAP definition of bronchiolitis: "a constellation of clinical symptoms and signs including a viral upper respiratory prodrome followed by increased respiratory effort and wheezing in children less than 2 years old."[22] The attending physician of record made the diagnosis. The ED physician–determined admission criteria included elements such as hypoxia (oxygen saturation <92% while awake), dehydration or failure to tolerate oral intake, tachypnea, or moderate to severe retractions demonstrating respiratory distress; a respiratory score was not a standard determinant of hospitalization. Inclusion criterion was infants <12 months old admitted with bronchiolitis. In accordance with the 2006 AAP definition of bronchiolitis,[22] we did not limit to the first episode of wheeze, unlike other studies. Age was <12 months to decrease the possibility of enrolling patients with asthma who may have an altered response to the study medication and require treatment with bronchodilators and/or systemic steroids, which would trigger withdrawal from the study. Exclusion criteria were continuing treatment of status asthmaticus (corticosteroids and/or bronchodilators), chronic cardiopulmonary disease (hemodynamically significant cardiac disease, chronic lung disease/bronchopulmonary dysplasia requiring diuretics or oxygen), cystic fibrosis, Trisomy 21, immunodeficiency/transplant recipient, neuromuscular disease, admission directly to the PICU, previous nebulized HS use <12 hours before presentation, non-English/non-Spanish speaker, and enrollment assessment >12 hours after admission. On first interim review by the data safety and monitoring board, another exclusion criterion was added: patients previously enrolled within 72 hours before presentation. Before this amendment, 2 patients enrolled in the HS group met this criterion; 1 reenrolled in the HS group and 1 in the NS group.

Study personnel interviewed parents/guardians by using a standardized eligibility questionnaire. After written informed consent, recruiters collected background and demographic information by using a standardized questionnaire, and Montefiore Medical Center Investigational Drug Services (IDS) randomized patients by using a computer-generated block randomization scheme (www.randomization.com, 1:1 allocation; random block sizes of 8). Composition of the study solutions prepared by IDS was not disclosed to medical personnel. Appearance and smell of the solutions were indistinguishable in sequentially numbered containers, with allocation concealed by IDS. The identity of study solutions and random assignment of patients by IDS to intervention group (3% HS) or control group (0.9% NS) was blinded to all study subjects, parents/guardians, medical care providers, and investigators. Study patients

received 4 mL nebulized study solution, either HS or NS based on assigned group, every 4 hours while remaining hospitalized. Patients could receive study treatment every 2 hours pro re nata (PRN), with a maximum of 2 PRN treatments per 24-hour period. Administration was via a Misty Max 10 nebulizer (Carefusion, Redlands, CA) with a pediatric vinyl under-the-chin aerosol mask connected to a standard hospital pressurized wall oxygen unit at 5 L/min (output 0.252 $\pm$ 0.009 g/min; aerodynamic mass median diameter 2.21 $\pm$ 0.07 μm).

Using the validated Respiratory Distress Assessment Instrument (RDAI),[23] investigators assigned patients a score before and 30 minutes after the first study treatment. RDAI functioned as a safety measure given theoretical risk of bronchospasm with HS,[24] not as an outcome measure, given its variable clinical utility.[25] If the RDAI score increased by $\geq$4 points, the patient received a bronchodilator to relieve bronchospasm and was withdrawn from the study (n = 1). At the time of study entry, we reviewed AAP guidelines regarding use of bronchodilator and systemic steroids with providers. We asked to withhold these treatments barring clinical deterioration during the study. In the event of clinical worsening, the provider had the option of giving an additional study treatment; if the provider felt bronchodilators or corticosteroids were indicated and administered one, the patient was withdrawn from the study (n = 8). Additional exit criteria included transfer to the PICU, and request of the parent/guardian.

Providers sent rapid virologic testing for respiratory syncytial virus (RSV) A and B, and influenza A and B, per routine hospital practice and clinician judgment. If rapid tests were negative or inconclusive, most patients had polymerase chain reaction testing for RSV, influenza, parainfluenza type 1, 2, 3, metapneumovirus, rhinovirus, and adenovirus per hospital practice.

The attending physician of record assessed patients daily, recorded any adverse events, and determined if the patient would remain hospitalized for a nonbronchiolitis-related indication altering LOS unless noted (eg, social concerns, other medical issues) (n = 5). Otherwise, patients could be discharged at any time of day as per hospital practice. The physician-determined discharge criteria included elements such as stable respiratory status without supplemental oxygen for at least 12 hours including with sleep, and sufficient oral intake to maintain hydration and urine output.

One week after discharge, research personnel conducted a standardized phone interview of the parent/guardian to determine if the patient had ongoing respiratory issues or was readmitted to any hospital for any reason.

This study was approved by the institutional review board of the Albert Einstein College of Medicine. A data safety and monitoring board reviewed interim data analyses throughout the study.

Outcomes

The primary outcome was LOS, defined as the time from first study treatment to the time of either the order for hospital discharge or meeting discharge criteria. This definition of LOS has greatest clinical relevance given variability of waiting times in the ED and the potential 12-hour window from time of admission to enrollment. A comparison LOS using admission order time to discharge order time was done for verification.

Secondary outcomes included total adverse events, subdivided as 7-day readmission rate and clinical worsening. We defined clinical worsening as transfer to the PICU, or bronchospasm within 30 minutes of a nebulized study treatment indicated by an increase/worsening of the RDAI[23] of $\geq$4 points. We systematically monitored for unforeseen adverse events (n = 0) throughout hospitalization and with a phone call 1 week after discharge.

Sample Size

Based on expert judgment and similar to a previous US study,[15] we determined a clinically meaningful decrease in LOS (primary outcome) to be 0.6 days. We estimated prestudy infant bronchiolitis LOS (time of triage presentation to departure time from the hospital) at 2.85 days based on hospital administrative data. For power analysis, we used PASS software (NCSS Statistical Software, Kaysville, UT) with 3 different types of adjustments (logistic, uniform, and normal distribution) and chose the most conservative to determine sample size. Based on these analyses, to achieve 80% power with a 2-tailed α = 0.05, we needed 105 patients in each group to identify a 0.6-day change in LOS. Initially, we estimated 10% attrition rate due to request by the parent/guardian, PICU transfer, or provider choice to use albuterol. During interim analysis, attrition rate approximated 20%, so we adjusted our target sample size to 126 patients per study group.

Statistical Analysis

We compared patient demographic and clinical characteristics between intervention and control groups by using χ^2 tests for categorical variables and t test for continuous normally distributed variables. We analyzed continuous non-normally distributed variables with Wilcoxon rank-sum tests. All tests were 2-sided (α = 0.05).

Given non-normally distributed LOS, we analyzed the difference in primary outcome (median LOS) between intervention and control groups with the Wilcoxon rank-sum test in an intention-to-treat analysis. To verify these findings, we performed a

per-protocol analysis to give the study medication the best chance of demonstrating effect if one existed. Using the same methods, we performed post hoc analyses of LOS for patients by RSV status, history of previous wheeze, prematurity, and study entry RDAI ≥4 or hypoxia. We performed analyses using Stata software version 12 (Stata Corp, College Station, TX).

We used Fisher's exact test to compare proportions of readmissions and adverse events. We used Fisher's exact test to compare between study groups the proportion of patients who received PRN study treatments and *t* test to compare mean change in RDAI score before and after initial study treatment.

RESULTS

We assessed 765 patients for eligibility and enrolled 227 subjects (Fig 1). Analyses were all by original assigned groups. There were no statistical differences between intervention and control groups for demographics and patient characteristics (Table 1). Of subjects with a race "Other," most parents/guardians identified the patient as Hispanic. Eighty of 190 patients who completed the study qualified as moderately ill based solely on RDAI score ≥4 on study entry. Additionally, of those with RDAI score <4, nearly half (49/110) were hypoxic, an element of clinical severity not evaluated in the RDAI score. A total of 37 patients withdrew from the study in the final per-protocol analysis (Fig 1); the proportion withdrawn was similar between intervention and control groups (17.6% vs 14.9%, respectively, $P = .59$) (Supplemental Table 5). Patient characteristics were similar between included and withdrawn patients, except for a higher proportion of patients with previous wheeze and prematurity in the withdrawn group (Table 2). We closed enrollment in the study after achieving a sample size of 227 patients because

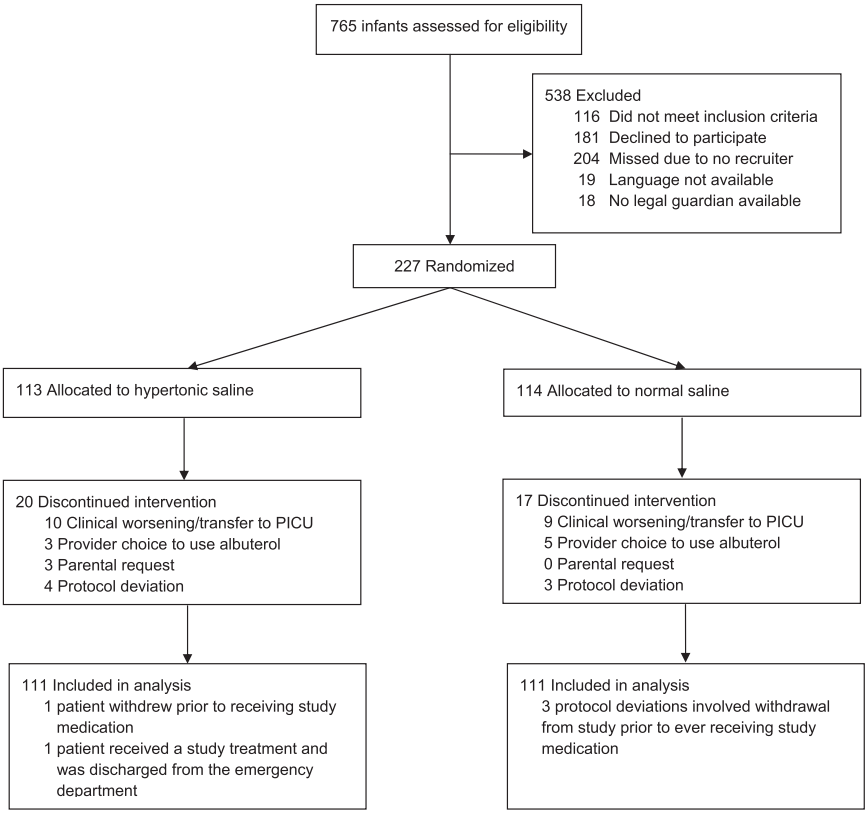

FIGURE 1
Patient enrollment flow diagram.

interim futility analysis indicated that neither arm could achieve superiority with further enrollment.

There was no difference in LOS between HS intervention and NS control groups by intention-to-treat analysis. The median LOS was 2.1 days in the HS group and 2.1 days in the NS group, $P = .73$ (Table 3). These findings were confirmed with a per-protocol analysis, demonstrating a median LOS of 2.0 days (interquartile range [IQR] 1.3–3.3) for HS and 2.0 days (IQR 1.2–3.0) for NS, $P = .96$. For further verification, we compared LOS calculated as time from admission order to discharge order. In this analysis, median LOS was 2.6 days (IQR 1.6–4.7) in the HS group and 2.5 days (IQR 1.6–3.9) in the NS group, $P = .76$.

There were no differences in readmission rates or adverse events between intervention and control groups (Table 3). Post hoc subgroup analyses by RSV infection, history of previous wheeze, history of prematurity, and those with study entry RDAI ≥4 or hypoxia, although underpowered, also found no differences in LOS between study groups (Table 4).

There was no difference when comparing mean change in RDAI before and after initial study treatment between study groups; mean change in score for HS was 0.21 and in NS was 0.18 ($P = .81$). Additionally, there was no difference in the proportion of patients who received PRN study treatments between HS and NS groups (8.6% vs 3.1%, $P = .13$).

No primary outcome (LOS) data were missing. Readmission rate had 10 missing data points (4 HS, 6 NS; Fisher's exact $P = .75$), due to inability to reach parents/guardians in follow-up phone call. There were no significant differences among those

TABLE 1 Baseline Characteristics of Patients Who Completed the Study by Treatment Group

Characteristics	3% HS, *n* = 93	0.9% NS, *n* = 97
Age, mo, mean ± SD	3.9 ± 3.0	4.4 ± 3.0
Male gender, *n* (%)	62 (67)	60 (62)
Race, *n* (%)		
Black	24 (26)	35 (36)
White	17 (18)	17 (18)
Other	48 (52)	41 (42)
Missing	4 (4)	4 (4)
Hispanic ethnicity, *n* (%)	71 (76)	71 (73)
Insurance, *n* (%)		
Medicaid	76 (82)	76 (78)
Private	12 (13)	14 (15)
No insurance	4 (4)	5 (5)
Other/missing	1 (1)	2 (2)
Viral status, *n* (%)[a]		
RSV	69 (74)	59 (61)
Another virus	13 (14)	13 (13)
Negative	7 (8)	13 (13)
RSV + another virus	2 (2)	5 (5)
No viral testing	2 (2)	7 (7)
Prior wheeze, *n* (%)	14 (15)	21 (22)
Premature, *n* (%)	11 (12)	15 (16)
Received steroids pre-study, *n* (%)	14 (15)	15 (16)
RDAI at study entry, mean ± SD	3.2 ± 2.3	3.5 ± 2.1
Prestudy days of symptoms, median (IQR)	5 (3–7)	4 (3–6)

[a] Due to rounding, proportions do not add to 100%.

missing (age/gender/race/ethnicity/prematurity/previous wheeze). Data are likely missing completely at random, but could bias our results if, for example, readmitted patients were less likely to be reached. We reanalyzed readmission rate, assuming those missing were readmitted: (1) all, (2) HS alone, or (3) NS alone, with no difference between study groups (P = .87, P = .13, P = .25, respectively).

TABLE 2 Baseline Characteristics of Included and Withdrawn Study Patients

Characteristics	Included, *n* = 190	Withdrawn, *n* = 37	*P*
Age, mo, mean ± SD	4.2 ± 3.0	3.5 ± 3.0	.21
Male gender, *n* (%)	122 (64.2)	26 (70.3)	.35
Race, *n* (%)[a]			.68
Black	59 (31.1)	13 (35.1)	
White	34 (17.9)	3 (8.1)	
Other	89 (46.8)	17 (45.9)	
Missing	8 (4.2)	4 (10.8)	
Hispanic ethnicity, *n* (%)	142 (74.7)	23 (62.2)	.73
Insurance, *n* (%)[a]			.32
Medicaid	152 (80.0)	28 (75.6)	
Private	26 (13.7)	7 (18.9)	
No insurance	9 (4.7)	0 (0.0)	
Other/missing	3 (1.6)	2 (5.4)	
Viral status, *n* (%)			.88
RSV	128 (67.4)	27 (75.7)	
Another virus	26 (13.7)	3 (8.1)	
Negative	20 (10.5)	3 (8.1)	
RSV + another virus	7 (3.7)	1 (2.7)	
No viral testing	9 (4.7)	2 (5.4)	
Prior wheeze, *n* (%)	35 (18.4)	9 (24.3)	<.001
Premature, *n* (%)	11 (13.7)	9 (24.3)	.014

[a] Due to rounding, proportions do not add to 100%.

DISCUSSION

This prospective, randomized double-blind controlled trial comparing HS with NS without bronchodilators in hospitalized children <12 months old, including those with previous wheeze, found no difference in LOS between groups. Additionally, HS was equivalent to NS in terms of adverse events, including clinical worsening and 7-day readmission.

These findings are similar to those in recent studies conducted both with and without concomitant bronchodilators in the United States[15] and abroad,[17,19] but contradict findings of several other published studies.[9,11–14] Our results challenge the conclusions of the most recent Cochrane review of HS,[18] which suggests a potential benefit of HS. We believe this is partly attributed to the 2 to 3 times longer average LOS in the latter studies[9,11–14] than in the studies in the United States and India. It is possible that HS has a greater effect when administered over a longer period of time than in an acute setting with a shorter LOS. A living systematic review incorporating studies since the Cochrane found overall decrease in LOS with HS.[26] However, subgroup analysis noted no difference in patients with LOS <3 days, consistent with our findings. Of note, several studies that were included used different HS concentrations and study entry points.

The Cochrane review of HS,[18] published while this study was enrolling, based recommendations on data from 1090 patients in 11 studies. Ours is the fifth negative study[15,17,19,20] since, totaling data from 1114 patients, demonstrating HS is not effective inpatient therapy for bronchiolitis.

Our study did not use bronchodilators and included patients with previous wheeze. Although we did not find that HS decreased LOS, we also did not find an increase in adverse events, including in a post hoc subgroup analysis (limited by being

TABLE 3 Primary Outcome: Intention-to-Treat Analysis of LOS; Secondary Outcomes: Total Adverse Events (7-Day Readmission Rate and Clinical Worsening) by Treatment Group

Variable	3% HS, *n* = 111	0.9% NS, *n* = 111	*P*
LOS, d, median (IQR)	2.1 (1.2–4.6)	2.1 (1.2–3.8)	.73
Total adverse events, *n* (%)[a]	14 (15)	12 (12)	.67
Readmissions, *n* (%)[a]	4 (4)	3 (3)	.77
Clinical worsening,[b] *n* (%)[c]	10 (9)	9 (8)	.97

[a] Total adverse events and readmissions were calculated out of patients who completed the study (HS *n* = 93 and NS *n* = 97), per institutional review board policy regarding follow-up of patients withdrawn from the study.

[b] Clinical worsening is defined as transfer to PICU (including withdrawals for use of bronchodilators who then transferred to the PICU), or RDAI increase of 4 or more points.

[c] All patients enrolled in the study were evaluated and included in the *n* for clinical worsening (HS *n* = 113, NS *n* = 114).

underpowered) of important subpopulations: those with prematurity, previous wheeze, RSV + bronchiolitis, or with study entry RDAI ≥4 or hypoxia. Despite previous concerns about administering HS to patients with a history of prematurity or previous wheeze, this study demonstrates both overall and in subgroup analyses safety of HS administration without bronchodilators. Of note, chronic lung disease was an exclusion criterion, which may confound interpretation of results of those with prematurity.

Bronchiolitis admissions consume substantial US health care resources, surpassing $1.7 billion annually in charges.[3] It is imperative that research focus on using effective treatments for these infants, minimizing bothersome interventions without benefit. Our negative study may help reduce use of HS and thereby decrease hospitalization costs and unnecessary resource utilization.

The primary limitation of this study was its single-center nature, raising the question of generalizability; however, LOS was comparable to other US studies on bronchiolitis,[3,15] and our results may be applicable to other urban centers with a diverse patient population. Second, enrolling patients within a 12-hour window from time of admission rather than on presentation could influence duration of time patients are in the study, especially for patients with a shorter LOS. However, this or even longer enrollment time frames were used in most other HS clinical trials.[9–13] A third limitation is no minimum severity score for eligibility; instead, admission to the hospital indicated severity of illness. Additionally, 42% of those completing the study had an RDAI score ≥4, and of 110 patients with scores <4, 45% were hypoxic before enrollment. There is also no difference in LOS in post hoc analysis of the subgroup of patients with RDAI ≥4 or hypoxia. Furthermore, the validity of respiratory scores, including RDAI, as a predictor of respiratory distress, disposition, and LOS is questionable,[25,27] suggesting a respiratory score may be a flawed study entry criterion. The 16% attrition rate might be considered a limitation; however, most withdrawals were for provider choice to use albuterol (not unexpected given our population's high endemic prevalence of asthma) or for PICU transfer (anticipated given natural course of illness). Additionally, although the mode of delivery was standardized, the approach to nebulized treatment administration in infants resisting was not and variability in administration to crying infants was possible. This likely reflects the reality of practice using nebulization in hospitalized infants. Finally, NS was the control instead of no treatment because HS lacks a true-blinded placebo. If NS reduces LOS in infants admitted with bronchiolitis, this may conservatively bias these results. Although a recent open study compares HS to supportive care alone,[19] for the purpose of blinding in this study and based on previous literature,[9–15,17] we used NS as a control. Additionally, although not a measure of cumulative effect of treatment, we found no difference in RDAI score before and after initial study treatment in the NS group, suggesting NS had no significant clinical effect.

TABLE 4 Post Hoc Subgroup Analysis for LOS by Treatment Group

Variable	3% HS	0.9% NS	*P*
RSV infection	*n* = 69	*n* = 59	
LOS, d, median (IQR)	2.2 (1.6–3.8)	2.0 (1.2–3.2)	.39
Previous wheeze	*n* = 14	*n* = 21	
LOS, d, median (IQR)	1.7 (1.1–2.6)	2.0 (1.2–3.2)	.18
Prematurity	*n* = 11	*n* = 15	
LOS, d, median (IQR)	2.9 (1.9–3.6)	2.2 (1.2–3.2)	.48
Entry RDAI ≥4 or hypoxia <92%	*n* = 62	*n* = 67	
LOS, d, median (IQR)	2.1 (1.3–4.1)	2.1 (1.3–3.7)	.83

CONCLUSIONS

This study found no difference in LOS in infants <1 year of age, including those with previous wheeze, admitted with bronchiolitis to a tertiary care center treated with nebulized HS as compared with those treated with NS without bronchodilators. HS is safe for use without adjunctive bronchodilators, including in those with a history of previous wheeze, as rates of adverse events were similar between study groups. Although including patients with previous wheeze may confound the diagnosis of bronchiolitis, a key finding from this study is that HS did not provoke bronchospasm. Future research could investigate effectiveness of higher saline concentrations, NS compared with supportive care alone, scheduled versus on-demand treatments, or 3% HS in the outpatient setting. This study suggests there is no utility for the routine use of 3% HS alone in treating

infants hospitalized with bronchiolitis as compared with NS.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ED: emergency department
HS: hypertonic saline
IDS: Investigational Drug Services
IQR: interquartile range
LOS: length of stay
NS: normal saline
PRN: pro re nata
RDAI: Respiratory Distress Assessment Instrument
RSV: respiratory syncytial virus

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