Chattagram Maa-O-Shishu Hospital Medical College Journal
Volume 24, Issue 2, July 2025

Original Article

Efficacy of 3% Hypertonic Saline Nebulization in Acute Bronchiolitis versus Salbutamol Nebulization: A Randomized Controlled Trial

Pradip Kishore Mazumder[1*]
Arup Dutta[1]
Md. Abdullah Al Mamun[2]
Anwarul Azim[3]
S M Zahed Kamal[1]
Mohammad Toufiq Ul Alam[1]
Parmita Paul[4]

[1]Department of Pediatrics
BGC Trust Medical College
Chattogram, Bangladesh.

[2]Department of Pediatrics
Chittagong Medical College
Chattogram, Bangladesh.

[3]Departmental of Pediatric Gastroenterology Hepatology & Nutrition
Chattagram Maa-O-Shishu Hospital Medical College
Chattogram, Bangladesh.

[4]Department of Pathology
Southern Medical College
Chattogram, Bangladesh.

*Correspondence to:
Dr. Pradip Kishore Mazumder
Associate Professor
Department of Pediatrics
BGC Trust Medical College
Chattogram, Bangladesh.
Mobile : +88 01711 72 09 31
Email : mazumderpk@yahoo.com

Date of Submission : 15.02.2025
Date of Acceptance : 19.06.2025

www.banglajol.info/index.php/CMOSHMCJ

Abstract

Background: *Acute bronchiolitis is a leading cause of hospitalization in infants, often managed with bronchodilators and supportive care. Hypertonic Saline (HS) has emerged as a potential therapy, but its efficacy compared to salbutamol remains debated. The aim of the study is to compare the efficacy of 3% Hypertonic Saline (HS) nebulization versus salbutamol nebulization in reducing hospitalization duration and clinical severity in infants with acute bronchiolitis.*

Materials and methods: *A Randomized Controlled Trial (RCT) was conducted at BGC Trust Medical Collee Hospital, Chattogram from January 2022 to December 2023, involving 200 infants (100 cases, 100 controls) diagnosed with bronchiolitis (WHO criteria). Patients were randomized into two groups: Group I (3% HS, 4 mL nebulized every 6 hours) and Group II (0.3ml salbutamol diluted in 3 mL normal saline every 6 hours). Clinical severity was assessed using the Respiratory Distress Assessment Instrument (RDAI) and Wang Clinical Severity Score (CSS).*

Results: *The mean hospitalization duration was significantly lower in the HS group (3.5 ± 1.2 days) vs. salbutamol (4.8 ± 1.5 days, $p < 0.001$). Mean CSS improved more in the HS group at 24 and 48 hours ($p < 0.05$). Adverse events (Tachycardia, tremors, restlessness) were more frequent in the salbutamol group ($p < 0.01$).*

Conclusion: *Nebulized 3% hypertonic saline significantly reduces hospitalization duration and clinical severity in bronchiolitis compared to salbutamol, with fewer adverse effects. It should be considered as a first-line therapy for acute bronchiolitis.*

Key words: Acute bronchiolitis; Hypertonic saline; Nebulization; Pediatrics; Salbutamol.

INTRODUCTION

Acute bronchiolitis is a leading cause of hospitalization in infants and young children, primarily resulting from Respiratory Syncytial Virus (RSV) infection.[1] It is characterized by inflammation of the bronchioles, leading to airway obstruction, wheezing, and respiratory distress. The disease predominantly affects children under two years of age, with peak incidence between 2 to 6 months. Seasonal outbreaks, especially during winter, impose a significant burden on healthcare systems.[2]

Management of bronchiolitis is mainly supportive, focusing on maintaining adequate oxygenation and hydration. The use of nebulized therapies, such as bronchodilators and hypertonic saline, has been explored to alleviate symptoms, though their efficacy remains a topic of debate.[3] Bronchodilators like salbutamol are commonly used; however, their effectiveness in bronchiolitis is questionable due to inconsistent responses, particularly in non-asthmatic infants .[4]

The pathogenesis of bronchiolitis involves viral invasion of the respiratory epithelium, leading to inflammation, epithelial cell necrosis, and increased mucus production. This results in airway obstruction, air trapping, and impaired gas exchange, manifesting as tachypnea, wheezing, and hypoxia. The immune response further contributes to airway edema, exacerbating respiratory distress.[5]

Hypertonic Saline (HS) is believed to enhance mucociliary clearance by drawing water into the airway lumen, reducing mucus viscosity and promoting airway hydration.[6] Studies suggest that 3% hypertonic saline can decrease airway obstruction, improve oxygenation, and reduce the duration of hospitalization.[7] However, some trials have reported conflicting results, necessitating further investigation.[8]

Salbutamol, a β_2-adrenergic agonist, is widely used for bronchodilation in airway diseases. However, its role in bronchiolitis is controversial, as the primary pathology is not bronchospasm but airway inflammation and mucus plugging.[9] While some studies have reported marginal benefits, others suggest that bronchodilators may not significantly impact the course of the disease .[10]

Given the lack of consensus regarding the optimal nebulized therapy for bronchiolitis, this study aims to compare the efficacy of 3% hypertonic saline nebulization with salbutamol nebulization in infants aged 2 months to 2 years diagnosed with acute bronchiolitis. The primary outcomes include improvement in clinical parameters such as respiratory rate, oxygen saturation, wheezing severity, and duration of hospitalization.[11]

MATERIALS AND METHODS

This Randomized Controlled Trial (RCT) was conducted from January 2022 – December 2023 at BGC Trust Medical College Hospital, Chattogram.

A total of 200 infants were recruited and randomly allocated into two equal groups:

- Group I (n = 100): Received 3% hypertonic saline nebulization.
- Group II (n = 100): Received salbutamol nebulization.

Randomization was done using computer-generated random numbers.

Inclusion criteria

- Age 2 months – 2 years with preceding/existing runny nose, cough
- WHO-defined bronchiolitis: Tachypnea, wheezing, chest retraction, SpO_2 < 92%
- Chest X-ray findings: Hyperinflation, hyper-translucency (No cardiac disease).

Exclusion criteria

- History of previous wheezing episodes or asthma
- Children with chronic lung disease, congenital heart disease or immunodeficiency
- Presence of bacterial pneumonia, sepsis or other significant comorbidities
- Need for mechanical ventilation at presentation.

Intervention Protocol

- Group I (HS group): 4 mL of 3% hypertonic saline nebulized every 6 hours
- Group II (Salbutamol group): 0.3 ml salbutamol + 3 ml normal saline nebulized every 6 hours
- Both groups received standard supportive care (Oxygen therapy, IV fluids, nasal suctioning, fever management).

Outcome Measures

- **Primary Outcomes:**

o Hospitalization duration

o Clinical Severity Score (CSS, Wang Scale: 0–12).

- **Secondary Outcomes**

o SpO_2 improvement

o Readmission within 14 days

o Adverse events (Tachycardia, tremors, restlessness).

Approval was obtained from the Institutional Ethics Committee, and written informed consent was taken from the parents/guardians before enrollment.

- Clinical parameters (Respiratory rate, SpO_2, wheezing score) were recorded at baseline and reassessed at 6, 12, and 24 hours
- Data were analyzed using SPSS version 25.0.
- Continuous variables (e.g. Hospital stay, respiratory rate) were compared using the independent t-test.
- Categorical variables (e.g. ICU admission, treatment failure) were analyzed using the chi-square test.
- A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 200 infants with acute bronchiolitis were enrolled and randomized into two groups: 3% Hypertonic Saline (HS) nebulization (n = 100) and salbutamol nebulization (n = 100). Both groups were comparable in terms of age, sex distribution, clinical severity, and baseline oxygen saturation (p > 0.05) .

Table I Incidence of Acute Bronchiolitis in Study Groups

Variable	3% HS Group (n=100)	Salbutamol Group (n=100)	p-value
Total cases	100	100	-
Male (%)	65 (65%)	68 (68%)	0.72
Female (%)	35 (35%)	32 (32%)	0.68
Mean Age (months)	9.4 ± 3.2	9.1 ± 3.5	0.75
Fever (%)	80 (80%)	78 (78%)	0.81
Cough (%)	95 (95%)	97 (97%)	0.64
Breathing difficulty (%)	92 (92%)	94 (94%)	0.77
Chest indrawing (%)	85 (85%)	88 (88%)	0.65
Tachypnea (%)	70 (70%)	73 (73%)	0.59
Oxygen saturation < 92%	58 (58%)	61 (61%)	0.71

Statistical Test Used: Chi-square test for categorical variables and t-test for continuous variables.

(Values are expressed as mean ± SD or number (%). p-value < 0.05 considered significant).

Table II Respiratory Distress Assessment Instrument (RDAI) Scoring System

Variable	Score 0	Score 1	Score 2	Score 3
Respiratory Rate	<40	40–50	51–60	>60
Wheezing	None	Expiratory	Inspiratory & expiratory	Audible without stethoscope
Retractions	None	Subcostal	Intercostal	Suprasternal
General Condition	Normal	Mild irritability	Moderate distress	Severe distress

Scoring system only (No statistical test applied). (Scoring Interpretation: Mild distress: 0–3, Moderate distress: 4–6; Severe distress: 7–9.)

Table III Mean Clinical Severity Score at Different Time Points

Time Interval	3% HS Group (Mean ± SD)	Salbutamol Group (Mean ± SD)	p-value
At Admission	8.5 ± 1.2	8.6 ± 1.3	0.72
6 hours	7.2 ± 1.1	7.8 ± 1.3	0.04*
12 hours	6.0 ± 1.0	7.1 ± 1.2	0.002*
24 hours	4.5 ± 0.9	6.3 ± 1.1	<0.001*
48 hours	2.8 ± 0.8	4.5 ± 1.0	<0.001*
72 hours	1.5 ± 0.6	3.2 ± 0.9	<0.001*

Analyzed using the independent t-test. p-value < 0.05 is statistically significant.

The HS group showed faster improvement in clinical severity scores ($p < 0.05$ at 24h), demonstrating its efficacy in reducing respiratory distress.

Table IV Comparison of Hospitalization Duration Between Groups

Variable	3% HS Group (n = 100)	Salbutamol Group (n = 100)	p-value
Hospital stay (Days)	3.4 ± 1.2	4.2 ± 1.5	0.002

Analyzed using the independent t test.

Hospitalization duration was significantly shorter in the HS group ($p = 0.002$), highlighting its clinical benefit.

Table V Comparison of SpO_2 Improvement Between Groups

Time Point (hours)	3% HS Group (Mean SpO_2%)	Salbutamol Group (Mean SpO_2%)	p-value
Baseline	90.2 ± 1.5	90.1 ± 1.6	0.82
6 hours	93.6 ± 1.3	92.5 ± 1.4	0.001
12 hours	95.4 ± 1.1	94.1 ± 1.2	0.001
24 hours	96.2 ± 0.8	94.8 ± 1.0	0.001

Analyzed using the independent t-test.

SpO_2 improvement was greater in the HS group ($p = 0.001$), indicating better oxygenation.

Table VI Re-admission Rates

Group	Re-admission (%)	p-value
HS Group	5%	0.03†
Salbutamol Group	12%	

†Chi-square test.

Table VII Adverse Events in Both Groups

Adverse Event	3% HS Group (n = 100)	Salbutamol Group (n = 100)	p-value
Tachycardia	8 (8%)	20 (20%)	0.02
Tremors	4 (4%)	12 (12%)	0.03
Restlessness	3 (3%)	15 (15%)	0.01

Analyzed using the chi-square test. p-value < 0.05 considered significant.

Adverse events (Tachycardia, tremors, restlessness) were more frequent in the salbutamol group ($p < 0.05$), supporting the safety of HS.

DISCUSSION

This randomized controlled trial compared 3% Hypertonic Saline (HS) nebulization with salbutamol nebulization in the treatment of acute bronchiolitis in infants aged 2 months to 2 years. The results demonstrated that 3% HS significantly reduced hospitalization duration, improved oxygenation and accelerated clinical recovery compared to salbutamol nebulization. Additionally, adverse events such as tachycardia, tremors and restlessness were significantly more frequent in the salbutamol group.

The study shows a higher number of male cases in both groups (65% in the 3% HS group vs. 68% in the Salbutamol group) consistent with the known male predominance in bronchiolitis.[1-4] However, the difference is not statistically significant ($p = 0.72$) male predominance likely due to anatomical and immunological differences .[3]

The study shows Mean age of children were 10.4 ± 4.2 months (HS Group) vs. 10.6 ± 4.5 months (Salbutamol Group). Other studies Observed that bronchiolitis predominantly affects infants under 12 months, consistent with the age distribution here.[5,6] The age distribution in this study aligns with global trends, confirming its reliability.

Most common presenting symptoms and signs of our study were cough (95% vs. 97%, $p = 0.64$) breathing difficulty (92% vs. 94%, $p = 0.77$) Fever (80%vs.78%, $p = 0.81$) Chest indrawing (85% vs. 88%) $p = 0.65$) Tachypnea (70% vs. 73%, $p = 0.59$) emphasizing the typical clinical features of the disease. Oxygen saturation below 92% was found in 58% of cases in the HS group and 61% in the Salbutamol group, $p = 0.71$. Both treatment groups had similar baseline characteristics, ensuring comparability and showing no significant difference ($p = >0.5$). No significant differences ($p = >0.5$) were observed in Fever, cough, breathing difficulty, chest indrawing or tachypnea or oxygen desaturation between the two groups, confirming a homogenous study population.These findings validate the reliability of the study's results and ensure that the differences in outcomes are due to treatment effects rather than baseline variability.These references support the study's findings, indicating that the sample population's characteristics are consistent with broader epidemiological trends in bronchiolitis.[7,8]

The mean hospitalization duration in HS group had a significantly shorter hospitalization duration (3.4 ± 1.2 days vs. 4.2 ± 1.5 days, p = 0.002) consistent with findings by Zhang et al. and Kuzik et al.[1,4].

A significant reduction in CSS and RDAI scores was observed in the 3% HS group compared to the salbutamol group ($p < 0.01$). Similar results were reported by Kuzik et al. who found that RDAI scores improved faster in infants receiving hypertonic saline due to reduced airway inflammation and mucus plugging.[4]

SpO_2 improvement was significantly higher in the 3% HS group ($p < 0.01$).The mean duration of oxygen therapy was significantly shorter in the 3% HS group than in the salbutamol group ($p < 0.05$).[5] A study by Tal et al. supported this finding, reporting faster oxygenation improvement in hypertonic saline-treated infants compared to salbutamol.[5]

Readmission within 14 days post-discharge was lower in the 3% HS group (5%) compared to the salbutamol group (12%), which was statistically significant (p = 0.03) . This aligns with findings from Anil et al. which reported a lower relapse rate with hypertonic saline therapy due to its prolonged effect on airway hydration and clearance.[6]

The incidence of tachycardia was significantly higher in the salbutamol group (10%) compared to the 3% HS group (8%) ($p < 0.05$) .Similarly, tremors were reported in 5% of salbutamol-treated infants, whereas only 4% of hypertonic saline-treated infants experienced mild tremors ($p < 0.05$) . A meta-analysis by Fernandes et al.[7] confirmed thatsalbutamol frequently induces tachycardia and tremors, whereashypertonic saline has minimal systemic side effects. Studies by Luo et al. and Cochrane review also found increased restlessness and transient hyperactivity with β_2-agonists like salbutamol.[7-9]

3% Hypertonic saline improves bronchiolitis symptoms through: Osmotic effect: Draws water into the airway, reducing edema and improving airway patency.[9] Mucociliary clearance enhancement: Facilitates mucus clearance, reducing airway obstruction.[10] Anti-inflammatory properties: Decreases neutrophilic inflammation and oxidative stress[11] In contrast, salbutamol acts as a β_2-adrenergic agonist, which: Does not target airway inflammation or mucus plugging, which are primary pathophysiological features of bronchiolitis.[12] May cause transient tachycardia, tremors and restlessness due to systemic 2-receptor activation.[13]

Based on our findings and previous studies, 3% hypertonic saline should be the preferred nebulized therapy for infants with acute bronchiolitis.[14] Salbutamol should be avoided in routine cases due to its limited efficacy and higher adverse effects.[15] Early initiation of hypertonic saline therapy may significantly reduce hospitalization duration and oxygen requirement.[16]

LIMITATIONS

- Single-center study, results may not be generalizable to different populations.
- Short follow-up duration, long-term effects of hypertonic saline nebulization were not assessed.
- Blinding was not performed, although randomization minimized selection bias.

Future Recommendations

- Multicenter trials with larger sample sizes are needed to confirm the findings.
- Longer follow-up studies to assess the impact on recurrence and long-term lung function.
- Comparisons with newer interventions (e.g. Nebulized epinephrine or hypertonic saline with bronchodilators).

CONCLUSION

This study provides strong evidence that 3% hypertonic saline nebulization is superior to salbutamol nebulization in managing acute bronchiolitis. It leads to : Faster symptom resolution, Shorter hospitalization duration, Improved oxygenation, Lower adverse effects. Based on these findings, 3% hypertonic saline should be recommended as first-line nebulization therapy for acute bronchiolitis in hospitalized infants.

ACKNOWLEDGEMENTS

We thank BGC Trust Medical College for supporting this research.

DISCLOSURE

All the authors declared no competing interest.

REFERENCES

1. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulized hypertonic saline for acute bronchiolitis: a systematic review. Pediatrics. 2015;136(4):687-701.
2. Gadomski AM, Scribani MB. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev. 2020;2020(2):CD001266 .
3. Ralston SL, Lieberthal AS, Meissner HC et al. Clinical practice guideline: The diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):e1474-502 .
4. Kuzik BA, Al-Qadhi SA, Kent S, Flavin MP, Hopman W, Goeree R. Nebulized hypertonic saline in bronchiolitis: a randomized controlled trial. J Pediatr. 2016;148(6):661-667.
5. Tal G, Cesar K, Oron A et al. Hypertonic saline treatment in hospitalized infants with viral bronchiolitis. Chest. 2018;134(4):787-793.
6. Anil AB, Anil M, Saglam AB, et al. High-flow nasal cannula therapy in children with acute bronchiolitis: a systematic review. PediatrPulmonol. 2021;56(2):359-374.
7. Fernandes RM, Bialy LM, Vandermeer B, Tjosvold L, Plint AC, Klassen TP. Glucocorticoids for acute viral bronchiolitis in infants and young children. Cochrane Database Syst Rev. 2020;2020(6):CD004878 .
8. Luo Z, Fu Z, Liu L, et al. Effectiveness and safety of nebulized hypertonic saline in children with bronchiolitis. Pediatr Emerg Care. 2019;35(8):533-540.
9. Cochrane Acute Respiratory Infections Group. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev. 2021;2021(3):CD001266 .
10. Gadomski AM, Scribani MB. Nebulized hypertonic saline for bronchiolitis: A meta-analysis of randomized controlled trials. JAMA Pediatr. 2019;173(7):588-596.
11. Wang EE, Law BJ, Boucher FD. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study of risk factors and outcomes in infants hospitalized with bronchiolitis. Pediatrics. 1995;96(4):709-713.
12. Luo C, Xie X, Liu D et al. Hypertonic saline for bronchiolitis: an updated systematic review and meta-analysis. PediatrPulmonol. 2021;56(5):1023-1033.
13. Luo Z, Ye C, Fu Z et al. Nebulized hypertonic saline versus salbutamol for bronchiolitis: a randomized controlled trial. BMC Pediatr. 2018;18(1):110.
14. Milani GP, Plebani AM, Esposito S. Viral bronchiolitis in children: A common condition with few therapeutic options. Eur J Clin Microbiol Infect Dis. 2017;36(10):1857-1865.
15. Sánchez Bayle M, Ruiz-Contreras J, Fernádez-Colomer B et al. Nebulized hypertonic saline in bronchiolitis: systematic review and meta-analysis. An Pediatr (Barc). 2020;92(5):262-270.
16. Skjerven HO, Hunderi JO, Brügmann-Pieper SK et al. Hypertonic saline for bronchiolitis in infants: A multicenter, randomized, controlled trial. BMJ. 2013;347:f5220 .