The Use of Hypertonic Saline Inhalation in Acute Bronchiolitis in Children

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Abstract:

Background: One medication that has promising results in managing acute bronchiolitis is nebulized hypertonic saline (HS). This work aimed to assess the role of HS in decreasing hospital stay in infants with acute viral bronchiolitis in Assiut University Children's Hospital.

Methods: This randomized clinical trial was carried out on 75 patients aged from two to 23 months old. 47 cases were male, and 28 were female, and they were diagnosed with bronchiolitis. Patients were divided into three equal groups; Group 1 was treated with a nebulized bronchodilator (salbutamol) and normal saline, Group 2 was treated with a nebulized bronchodilator (salbutamol) and HS, and Group 3 was treated with nebulized HS only.

Results: The three groups of children had the same pertinent baseline clinical characteristics. All groups had a highly statistically significant difference regarding the duration of illness before study entry (days). There was no significant difference between all groups regarding clinical severity scores before treatment, and there was a significant decrease in clinical severity scores after treatment among the three groups. There was a statistically significant difference between all groups regarding the length of hospital stay, whereas there was no significant difference between groups I and II. There was a highly significant decrease among Group II than Group I, and there was a highly significant decrease among Group III than Group I.

Conclusions: Nebulization with HS reduces the length of stay in the hospital and decreases the clinical severity score in children hospitalized with viral bronchiolitis.

Keywords: Acute Bronchiolitis, nebulization, Hypertonic Saline Inhalation.

Introduction

Acute bronchiolitis, predominantly affecting children under two, is a viral infection marked by respiratory distress, wheezing, and crackles [1]. While it often resolves on its own, it can escalate to severe conditions like apnea or respiratory failure. The primary culprit is the respiratory syncytial virus (RSV), though other viruses, such as human metapneumovirus and adenovirus, also contribute [1].

The disease's pathogenesis involves acute inflammation, swelling beneath the mucosa, destruction of airway epithelial cells, hindered mucus clearance due to dehydration on the airway surface, increased mucus production, and bronchospasm [2]. Given the viral nature of bronchiolitis, specific antiviral treatments are largely ineffective, leaving symptom management, hydration, and oxygenation as the mainstays of care [2]. Despite extensive research, oxygen therapy remains the only intervention with a significant impact on young patients' recovery, with the efficacy of other treatments still under debate.

Nebulized hypertonic saline (HS) has gained attention for its potential benefits in managing acute bronchiolitis [3]. Its high osmolarity helps draw water out from the mucosal and submucosal layers, thereby improving mucociliary clearance by loosening fluid and mucus accumulations in the airways [3]. Additionally, HS can provoke coughing, further aiding in clearing mucus [3]. The American Academy of

Pediatrics endorses HS use for hospitalized patients with bronchiolitis, noting its ability to alleviate symptoms within 24 hours of treatment initiation and shorten hospital stays for those expected to be admitted for over three days [4]. HS might also lower the rates of emergency department admissions. However, its effectiveness for severe cases in intensive care remains underexplored [5]. Given its safety and efficacy, HS, particularly in a 3% concentration administered every 4 to 6 hours via nebulizer, is recommended for mild-to-moderate bronchiolitis management, with treatment continuing throughout hospitalization [6].

Research indicates that nebulized HS can reduce hospitalization time by nearly 10 hours compared to NS, slightly improve clinical severity scores, and decrease the risk of hospitalization by 13% for outpatient or emergency department-treated children [7, 8]. Minor and self-resolving side effects like increased coughing and agitation have been observed, especially when combined with bronchodilators [8]. Despite these promising findings, the evidence's reliability is considered low to very low, highlighting the need for further large-scale studies to confirm these benefits [7].

Aim: To evaluate the effectiveness of nebulized HS in reducing the duration of hospitalization for infants with acute viral bronchiolitis at Assiut University Children's Hospital.

Patients and Methods:

Clinical trial number: NCT03880903.

In this randomized clinical trial, 75 patients diagnosed with bronchiolitis were enrolled. The study population consisted of 47 male and 28 female patients, ages 2 to 23 months. To evaluate the effectiveness of different treatment approaches, the patients were randomly allocated into three groups of equal size:

1. Group 1 (Control Group): This group received a combination of nebulized bronchodilator (salbutamol) and NS. Salbutamol, a short-acting β2-adrenergic receptor agonist, was administered to relax the smooth muscles of the airways, while NS was used as a vehicle for nebulization.
2. Group 2 (Bronchodilator + Hypertonic Saline Group): Patients in this group were treated with a combination of nebulized salbutamol and HS. Adding HS to the treatment regimen was intended to reduce mucus viscosity, improve mucociliary clearance, and decrease airway oedema.
3. Group 3 (Hypertonic Saline Group): This group received nebulized HS alone without adding a bronchodilator. This group aimed to assess the effectiveness of HS as a standalone treatment for bronchiolitis, evaluating its potential to improve clinical outcomes without the need for bronchodilator therapy.

All patients were subjected to:

- Full history taking (Name, age, sex, present and past history, family history), clinical examination (general and systemic examination including Vital signs: pulse, temperature, and respiratory rate, and head and neck examination: cyanosis and working ala nasi).
- Chest examination: Inspection: respiratory rate, chest wall deformities, and respiratory distress score; palpation: position of the mediastinum (tracheal palpation and apical beat), percussion: for resonance, dullness, or hyper-resonance; auscultation: Air entry, crepitation, and wheezes.
- Investigations: Chest X-ray: PA (Posteroanterior) and lateral view.
- The Clinical Severity Score (CSS) is a standardized tool used to determine the severity of bronchiolitis in infants and young children by assessing four clinical indicators: respiratory rate, wheezing, chest retraction, and general condition. Each indicator is scored from 0 to 3, with higher scores indicating more severe symptoms. A respiratory rate below 30 breaths per minute scores a 0, while over 60 breaths per minute scores a 3. Wheezing is scored from 0 for none to 3

for wheezing during both inspiration and expiration. Chest retraction scores range from 0 for none to 3 for severe retraction with nasal flaring. The general condition is scored as 0 for normal and 3 for symptoms like irritability or poor feeding. The total CSS can range from 0 to 12, with scores of 0-3 indicating mild, 4-8 moderate, and 9-12 severe bronchiolitis. This tool aids clinicians in evaluating the illness's severity and guiding treatment decisions **[9].**

Statistical Analysis:

In the study, data analysis was conducted using SPSS version 20. Quantitative data, represented as mean and standard deviation (SD), were analyzed within each group using the paired Student's t-test to identify significant differences. For qualitative data, which were presented as frequency and percentage (%), the Chi-square test and/or Fisher's exact test were employed for comparison. One-way ANOVA was utilized when comparing more than two independent groups with quantitative data with a parametric distribution. A two-tailed P-value of less than 0.05 was deemed to indicate statistical significance. This approach allowed for a comprehensive analysis of the study's quantitative and qualitative aspects, ensuring a robust examination of the data to draw meaningful conclusions.

Ethical Consideration: The study received approval from the Ethical Committee of Assiut University Children's Hospital in Egypt, ensuring adherence to ethical standards in medical research. Written informed consent was obtained from the relatives of the patients to participate in the study, demonstrating respect for patient rights and ethical considerations in clinical research.

IRB No.: 1710068.

Results:

Table 1: Patient characteristics, residence, and gestational age of the studied patients

		Patients
Age (Months)		14.72 ± 5.91
Sex	Male	47 (62.7%)
	Female	28 (37.3%)
Residence	Rural	30 (40%)
	Urban	45 (60%)
Gestational Age	Full-term delivery	73 (97.3%)
	Premature delivery	2 (2.7%)

Data are presented as mean ± SD or frequency (%).

Table 2: Comparison between 3 Groups regarding clinical symptoms, physical and radiological findings

Symptoms		Total		Group I		Group II		Group III		Test value*	P-value	Sig.
		No.	%	No.	%	No.	%	No.	%			
Cough	No	15	20%	6	24%	6	24%	3	12%	1.500	0.472	NS
	Yes	60	80%	19	76%	19	76%	22	88%			
Runny nose	No	26	34.7%	8	32%	10	40%	8	32%	0.471	0.790	NS
	Yes	49	65.3%	17	68%	15	60%	17	68%			
Irritability	No	38	50.7%	13	52%	13	52%	12	48%	0.107	0.948	NS
	Yes	37	49.3%	12	48%	12	48%	13	52%			
S.O.B	No	17	22.7%	6	24%	5	20%	6	24%	0.152	0.927	NS
	Yes	58	77.3%	19	76%	20	80%	19	76%			
Poor feeding	No	37	49.3%	10	40%	13	52%	14	56%	1.387	0.500	NS
	Yes	38	50.7%	15	60%	12	48%	11	44%			
Temperature	>39	31	41.3%	12	48%	8	32%	11	44%	3.629	0.727	NS
	37.4-38	18	24.0%	6	24%	5	20%	7	28%			
	38.1-39	21	28.0%	6	24%	9	36%	6	24%			
	Afebrile	5	6.7%	1	4%	3	12%	1	4%			

Symptoms		Total		Group I		Group II		Group III		Test value*	P-value	Sig.
		No.	%	No.	%	No.	%	No.	%			
Fine rales	No	28	37.3%	10	40%	8	32%	10	40%	0.456	0.796	NS
	Yes	47	62.7%	15	60%	17	68%	15	60%			
Sibilent rhonchi	No	13	17.3%	3	12%	5	20%	5	20%	0.744	0.689	NS
	Yes	62	82.7%	22	88%	20	80.0%	20	80%			
Severe retraction	No	23	30.7%	6	24%	9	36%	8	32%	0.878	0.645	NS
	Yes	52	69.3%	19	76%	16	64%	17	68%			
Nasal flaring	No	49	65.3%	18	72%	16	64%	15	60%	0.824	0.662	NS
	Yes	26	34.7%	7	28%	9	36%	10	40%			
Cyanosis	No	64	85.3%	22	88%	21	84%	21	84%	0.213	0.899	NS
	Yes	11	14.7%	3	12%	4	16%	4	16%			
Apnea	No	72	96%	24	96%	24	96%	24	96%	0.000	1.000	NS
	Yes	3	4%	1	4%	1	4%	1	4%			
Hyperinflation	No	45	60%	14	56%	14	56%	17	68%	1.000	0.607	NS
	Yes	30	40%	11	44%	11	44%	8	32%			
Interstitial Pneumonia	No	58	77.3%	19	76%	20	80%	19	76%	0.152	0.927	NS
	Yes	17	22.7%	6	24%	5	20%	6	24%			
Consolidation	No	63	84%	22	88%	20	80%	21	84%	0.595	0.743	NS
	Yes	12	16%	3	12%	5	20%	4	16%			
Normal x-ray	No	56	74.7%	17	68%	20	80%	19	76%	0.987	0.611	NS
	Yes	19	25.3%	8	32%	5	20%	6	24%			

The analysis revealed no statistically significant differences between the groups regarding infants treated with bronchodilators, steroids, or antibiotics before the commencement of the study. This indicates that the prior administration of these treatments did not significantly impact the outcomes measured across the different study groups, suggesting a uniform baseline for these specific interventions among the participants.

Table 4: Comparison between three groups regarding duration of illness before study entry (days)

	Group I	Group II	Group III	Test value•	P-value	Sig.
	No. = 25	No. = 25	No. = 25			
Duration of illness before study entry (days)	2.94 ± 0.89	2.18 ± 0.64	3.13 ± 0.84	9.824	0.000	HS
	Post hoc analysis			–	–	–
	P1	P2	P3	–	–	–
	0.001	0.400	0.000	–	–	–

P1, P2, and P3 are the p-values of groups I, II, and III, respectively, compared to the p-value result from the ANOVA test; the post hoc test was done only if the ANOVA test was significant.

The study found a highly statistically significant difference between the groups regarding the duration of illness before entering the study. This suggests that the length of time each patient had been experiencing symptoms before the study varied significantly across the groups, which could be an important factor in the study's analysis and outcomes.

Table 5: Comparison between 3 Groups regarding CS scores

CS scores	Group I	Group II	Group III	Test value•	P-value	Sig.
	No. = 25	No. = 25	No. = 25			
Before Treatment	5.49 ± 0.71	5.61 ± 1.07	5.17 ± 1.32	1.187	0.311	NS
After Treatment	3.48 ± 0.41	1.17 ± 0.46	2.04 ± 0.73	112.887	0.000	HS
	Post hoc analysis			–	–	–
	P1	P2	P3	–	–	–
Before Treatment	0.675	0.287	0.139	–	–	–
After Treatment	0.000	0.000	0.000	–	–	–

P1, P2, and P3 are the p-values of groups I, II, and III, respectively, compared to the p-value result from the ANOVA test; the post hoc test was done only if the ANOVA test was significant.

The study revealed no statistically significant difference in CSS among the groups studied before treatment. This indicates that the initial severity of bronchiolitis was comparable across all groups involved in the research. However, after the treatment was administered, a highly statistically significant difference in CSS scores was observed between the groups. This suggests that the treatments had varying levels of effectiveness in managing bronchiolitis, leading to different outcomes in terms of disease severity reduction across the studied groups. The findings underscore the importance of evaluating different treatment modalities' effectiveness in reducing bronchiolitis symptoms' severity and improving patient outcomes.

Table 6: Comparison between three Groups regarding CS scores

CS scores	Before Treatment	After Treatment	Test value•	P-value	Sig.
	No. = 25	No. = 25			
Group I	5.49 ± 0.71	3.48 ± 0.41	13.733	0.000	HS
Group II	5.61 ± 1.07	1.17 ± 0.46	21.280	0.000	HS
Group III	5.17 ± 1.32	2.04 ± 0.73	11.435	0.000	HS

The study demonstrated a highly statistically significant difference in CSS among all groups when comparing scores before and after treatment. This indicates that the treatment significantly impacted the severity of the symptoms, as measured by the CSS, across all groups involved in the study.

Table 7: Comparison between 3 groups regarding length of hospital stay (Days)

	Group I	Group II	Group III	Test value	P-value	Sig.
	No. = 25	No. = 25	No. = 25			
Length of hospital stay (Days)	5.18 ± 0.91	3.38 ± 1.03	3.73 ± 1.23	20.015	0.000	HS
	Post hoc analysis			–	–	–
	P1	P2	P3	–	–	–
	0.000	0.000	0.248	–	–	–

P1, P2, and P3 are the p-values of groups I, II, and III, respectively, compared to the p-value result from the ANOVA test, the post hoc test was done only if the ANOVA test was significant.

The study identified a highly statistically significant difference in the length of hospital stay among the studied groups. This indicates that the duration of hospitalization varied significantly between the groups, suggesting that the interventions or conditions being compared had a notable

impact on how long patients remained in the hospital.

Discussion

Over the last decade, a significant body of research has supported the application of nebulized HS as a strategy to shorten the course of respiratory conditions and, as a result, reduce the length of hospital admissions [10]. It's believed that HS can make bronchial mucus less thick, decrease swelling in the airways, and enhance the efficiency of mucus clearance by cilia. Moreover, HS is thought to positively affect the mucus-clearing ability of cilia in both normal and compromised lung conditions [11].

At the start of the study, the demographic and clinical profiles of the children across the three groups were closely aligned, reflecting the findings of Elesh et al. [6] and aligning with the age comparability noted by Teunissen et al. [12]. Our study revealed significant enhancements in CSS post-treatment across all groups, with the combination of nebulized bronchodilator (salbutamol) and HS marking the most notable improvement in CS, and group I showing minimal improvement. This is consistent with the outcomes reported by Elesh et al. [6], who noted benefits with 3% nebulized HS. A decrease in respiratory rate was observed in both groups, yet improvements in oxygen saturation were more pronounced after 72 hours in the 3% HS group. The period required for oxygen therapy was markedly shorter in the HS group compared to the group treated with NS [6].

In a controlled trial, combining HS with racemic epinephrine proved more effective than nebulized NS with racemic epinephrine, administered three times daily until discharge in a cohort of 52 infants with bronchiolitis [13]. Those receiving a 3% HS solution exhibited a 25% improvement in mean CSS by the third day compared to those treated with NS [13]. Conversely, some studies have not observed immediate clinical advantages with nebulized HS, and neither 3% nor 6% HS led to a reduction in the CSS at discharge nor the duration of supplemental oxygen or tube feeding compared to NS [14]. Sharma et al. also found no significant difference in CSS between 3% HS and 0.9% saline groups, and two extensive multicenter European trials reported unfavorable outcomes for nebulized HS compared with NS [15].

A meta-analysis has pointed out a possible inverse relationship between bronchiolitis severity and nebulized HS's effectiveness, suggesting that the varying severity levels in different study populations might explain the inconsistent responses to HS treatment [11]. The study showed a notable statistical difference in the length of hospital stays among the groups. Specifically, the group treated with nebulized bronchodilator (salbutamol) and NS had the longest average hospital stay of 5.18 days, while the group treated with nebulized bronchodilator (salbutamol) and HS had the shortest stay, averaging 3.38 days, followed by the group that received only nebulized HS at 3.73 days. These findings align with those of Elesh et al. [6], who observed that 3% HS significantly cut down the duration of hospitalization, with most patients being discharged within three days of starting treatment. Similar reductions in hospital stay duration were noted in two other studies that compared HS treatment groups [16, 17].

Other researchers have also reported that using HS in infants with bronchiolitis can significantly shorten the length of hospital stays compared to NS [18, 19]. A recent review of clinical trials concluded that nebulized 3% saline could significantly decrease hospitalization time and improve CSS [11]. In a double-blind, randomized controlled trial, HS combined with racemic epinephrine was more effective than nebulized NS with racemic epinephrine, administered three times daily until discharge for infants with bronchiolitis, leading to a 25% reduction in hospital stays [13].

A meta-analysis indicated an approximate one-day reduction in hospital stay for patients treated with nebulized HS compared to those who received NS [3].

Badgett et al. found a significant correlation between the duration of therapy and the efficacy of HS, suggesting a threshold effect after more than three days of treatment [20]. However, Al-Ansari et al. did not observe an effect on the duration of hospital stay, attributing it to various medical and social factors [16], and Teunissen et al. reported that neither 3% HS nor 6% HS reduced the hospital stay duration compared to NS [11]. A randomized controlled trial also showed no significant difference in the hospital admission rate or length of stay between groups treated with nebulized HS and NS [17]. Sharma et al. revealed that the average hospital stay was similar between the 3% saline and 0.9% saline groups, suggesting that nebulized 3% HS was not superior to 0.9% saline in infants with diagnosed bronchiolitis [15]. Pandit et al. concluded that nebulization with HS plus adrenaline and NS plus adrenaline were equally effective in treating bronchiolitis in infants [21].

Considering the results of this study and others, both supporting and opposing, HS appears to be a valuable treatment option for bronchiolitis, particularly for mild to moderate cases in emergency departments. It is recommended that further comprehensive studies be conducted to evaluate the efficacy of HS fully. The use of HS inhalation, either with salbutamol or alone, is suggested, and additional research with a larger number of patients is needed to confirm these findings and improve patient outcomes.

Conclusions

The study demonstrates that nebulization with HS effectively reduces the length of hospital stay and the CSS in children hospitalized with viral bronchiolitis. Group II, which received HS nebulization, showed the most significant improvements among the groups studied. These findings highlight the potential of HS nebulization as a beneficial treatment strategy for managing viral bronchiolitis in hospitalized children, offering a promising approach to enhance patient outcomes and reduce the burden on healthcare facilities.

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