

Original Article

Management of Bronchiolitis with mucolytic agent (3% NaCl) in children in a hospital in Dhaka City without antibiotic

*Sudipta Roy¹, ARM Luthful Kabir², Kazi Selim Anwer³, Rahat Bin Habib⁴, Masuma Khan⁵

Abstract

Background: Bronchiolitis is mostly a viral disease of lower respiratory tract in infants and young children. Variation in the management has been documented. Treatment with 3 % hypertonic saline has a significantly shorter mean length of hospital stay and improved clinical severity score. Antibiotic has little role in the management of bronchiolitis though it is invariably prescribed. However, management of bronchiolitis is yet not optimized according to recommendation.

Objective: To evaluate the outcome of bronchiolitis with 3% NaCl nebulization without antibiotic.

Methodology: This observational study was conducted in Ad-din Medical College Hospital at the department of pediatrics during October, 2018 to January, 2019. Among 92 cases of clinically diagnosed bronchiolitis 30 were excluded due to prior antibiotic therapy and rest 62 cases were enrolled based on inclusion criteria (age below 2 years, 1st or 2nd episode of wheeze, runny nose, cough, respiratory distress, wheeze/ ronchi, hyperinflation / increased translucency on CXR). Consent of the parents was taken. A structured questionnaire was filled up. Detailed history was taken and full physical examination was done. CBE with PBF, CRP & CXR were done immediately after admission. All children were managed with 6 hourly 3% NaCl nebulization in addition to supportive measures whenever indicated like IV 5% dextrose in 0.225% saline, O₂ inhalation, paracetamol for fever and were followed 8 hourly. Patients were discharged after returning of social smile, absence of feeding difficulty, fast breathing and free of O₂ therapy. However, thirty cases were taken out of the study for increased severity or persistence of symptoms. So finally data were analysed in 32 cases using SPSS 22.

Results: Mean age of presentation was 5 months, 75% in male children. Cough and respiratory distress were present in 100 % cases, wheezing (71%), runny nose and absence of social smile in 56% cases, fever (53%), feeding difficulty (50%), vomiting (28%) sleeping difficulty (25%), subcostal recession (100%) fast breathing (68%), mouth breathing (45%), nasal flaring (40%), intercostal recession (9%), low grade fever (37%), SPO₂ < 90% (71%), vesicular breath sound with prolong expiration (75%), bilateral ronchi (100%), bilateral crepitation (15%). Total leucocyte count was normal (<15,000/cmm) in 75%, lymphocytosis was found in 81%, CRP was negative (<6) in 68%. On CXR-increased translucency (100%), hyperinflation (100%), sticky density (12%) upper lobe collapse consolidation (6%). Intra venous fluid was given in 43%, O₂ therapy (81%), mean duration of O₂ therapy was 3 days and mean duration of clinical improvement or hospital stay was 4 days.

Conclusion: Nebulized hypertonic saline solution (3% NaCl) was found effective without antibiotic therapy in acute bronchiolitis. Therefore, routine use of antibiotic is prohibited.

Key words: Bronchiolitis, 3% NaCl, antibiotics

1. *Associate Professor, Dept. of Pediatrics, Ad-din Women's Medical College & Hospital(AWMCH)
2. Professor, Dept. of Pediatrics, Ad-din Women's Medical College & Hospital (AWMCH)
3. Head, Medical Research Unit, Ad-din Women's Medical College & Hospital (AWMCH)
4. Assistant Professor, Dept. of Pediatrics, Shahid Syed Nazrul Islam Medical College, Kishoreganj
5. Associate Professor, Dept of Pediatrics, Ad-din Women's Medical College & Hospital (AWMCH)

Correspondence: Dr. Sudipta Roy, Associate Professor, Dept. of Pediatrics, Ad-din Women's Medical College & Hospital(AWMCH), E-mail: sudipta.paediatrics@gmail.com

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Introduction

Around 95% cases of bronchiolitis are of viral origin and Respiratory syncytial virus(RSV) is the commonest one,^{1,2} ranging from 50% to 91%.^{3,4} Epidemiological studies have revealed the association of bronchiolitis with a high degree of morbidity but low mortality.⁵

Because of the paucity of available therapeutic options, recent literature has focused on novel therapies, such as hypertonic saline, for the management of bronchiolitis. The pathology of bronchiolitis involves acute inflammation, edema and necrosis of epithelial cells and increased mucus production.⁶ Mucus plugs in the airway produce partial or total air flow obstruction resulting in

atelectasis which may further worsen the breathing and respiratory function. In bronchiolitis, there is increased sodium absorption and dehydration of airway resulting in impairment of mucus clearance.^{5,6} Substances that improves mucus clearance should be beneficial in resolving bronchiolitis. Hypertonic saline plays an important role in bronchiolitis by shifting the flow of water into the mucus layer by osmosis, reducing sub mucosal edema and viscosity of mucus, thereby improving mucus clearance, and rehydrating the air surface.^{7,8,9,10} The updated American Academy of Pediatrics (AAP) guidelines support the use of hypertonic saline nebulization for infants and children hospitalized for bronchiolitis.¹¹ On the other hand, Most paediatricians are anxious about not using antibiotics and they invariably prescribe antibiotics for bronchiolitis¹² often being confused with pneumonia.¹³

Taking into account the fact that antibiotics are no longer recommended in bronchiolitis, though we are using it invariably and a certain number of studies showed the therapeutic effect of 3% NaCl nebulization, this observational study was conducted to evaluate the outcome of bronchiolitis with 3% NaCl in addition to other supportive measures but without antibiotics and compared our results with existing literatures.

Materials and Methods

This observational study was conducted in Ad-din Medical college Hospital, Dhaka, Bangladesh at the department of Pediatrics during October, 2018 to February, 2019 over a period of 5 months.

Total sample size: Initially 110 cases of clinically diagnosed bronchiolitis were enrolled for this study. Among 110 cases, 30 were excluded due to prior antibiotic therapy. Rest 80 cases fulfilled the inclusion criteria. However, another 30 cases were taken out during ongoing treatment. Among these 30 cases, few were referred to hospital with PICU support for increased severity of distress and falling oxygen saturation as we did not have PICU facilities, in some cases antibiotic was added suspecting secondary bacterial infection based on high fever and complete blood count and few parents quit the study. So, finally study was done in 50 cases.

Inclusion criteria: Any child below 2 years of age having first or 2nd episode of bronchiolitis based on cough, respiratory distress, wheeze/ronchi on auscultation,¹³(137, National guideline, 2005) hyperinflation & or increased translucency on CXR without prior antibiotic therapy.

Exclusion criteria: Children with recurrent wheeze (3 or more), atopic condition, congenital heart disease,

possible immune-deficiency and prior antibiotic therapy were excluded.

After enrollment, informed written consent was taken from the parents. A structured questionnaire was filled up. Detailed history was taken and full physical examination was done.

Investigations: CBC, PBF, CRP, CXR were done immediately after admission.

Treatment: All children were managed with 6 hourly 3% NaCl nebulization. Other supportive measures: Oxygen inhalation, IV 5% dextrose in 0.225% NaCl, Paracetamol for fever were given whenever **indicated**.

Follow - Up: 8 hourly until discharged.

Outcome Variables: Returning of social smile, no feeding difficulty, no fast breathing, no oxygen requirement in room air.

Statistical analysis: Ethical implications: Ethical considerations were taken into account at every stage. The study was approved by Ethical Review Committee, Ad-din Medical College Hospital. Anonymity of children and confidentiality of medical records were ensured. Written informed consent was secured from parents and their liberty of withdrawing child from the study at any point was ensured.

Results:

Table- I showing demographic characteristics of cases. Mean age of children was 5.07 ± 3.6 months, and 76% were boys, M: F - 3.1:1, exclusive breast feeding was given in 64%, 44% were exposed to passive smoking and 74% had WHZ < -2SD.

Table-I: Demographic Characteristics of Cases:

	Characteristics	Frequency (%)
Age	0-6 Months	36 (72%)
	By 7-12 Months	11 (22%)
	By 13-18 Months	3 (6%)
Mean Age	5.07 ± 3.6 Months	
Sex	Male (M)	38 (76%)
	Female (F)	12 (24%)
M: F	3.1:1	
Pre Term (PT), Low Birth Weight (LBW)		5 (10%)
Exclusive Breast Feeding (EBF)		32 (64%)
Exposure to Passive Smoking		22 (44%)
WHZ	<-2	37 (74%)
	-2-3	6 (12%)
	>-3	7 (14%)

Diagnosis of bronchiolitis was based on cough, respiratory distress (fast breathing), subcostal recession, bilateral ronchi, hyperinflation and increased translucency on CXR, that were present in 100% cases. (Table-II).

Table –II: Diagnostic Criteria:

Variables	Frequency (%)
Cough	50 (100%)
Respiratory Distress	50 (100%)
Subcostal Recession	50 (100%)
Bilateral Ronchi	50 (100%)
Hyperinflation on CXR	50(100%)
Increased Translucency on CXR	50(100%)

Other common symptoms were fever (60%), runny nose (56%), wheezing (76%), feeding difficulty (44%), sleeping difficulty (18%) and absence of social smile in 50% cases. (Table-III).

Table –III: Common Symptoms

Symptoms	Frequency
Fever	30 (60%)
Running Nose	28 (56%)
Wheezing	38 (76%)
Vomiting	16 (32%)
Loose Motion	10 (20%)
Feeding Difficulty	22 (44%)
Sleeping Difficulty	9 (18%)
No Social Smile	25 (50%)

Physical findings revealed distressed look in 68%, fast breathing (100%), mean respiratory rate 54.02 ± 12.5 , mean temperature 98.9 ± 1.41 (Table-IV).

Table –IV: Physical Findings

Physical Findings	Frequency (%)
Distressed	34 (68%)
Playful	21 (42%)
Respiratory Rate (mean)	54.02 ± 12.5
Fast Breathing	36 (72%)
Nasal Flaring	14 (28%)
Mouth Breathing	16 (32%)
Intercostal Recession	7 (14%)
Suprasternal Recession	4 (8%)
Low Grade Fever (99-100F)	5 (10%)
High grade Fever (101-104F)	5 (10%)S

PO₂ < 90% in 76% cases, mean SPO₂ was 87.5 ± 7.5 , breath sound vesicular with prolong expiration in 76% cases. (Table-V).

Table-V: Physical Findings

Physical Findings		Frequency (%)
SPo ₂	Mean	87.5 ± 7.5
	<90%	38 (76%)
	>90%	12 (24%)
Hyper resonant on Percussion		12 (28%)
Breath Sound Vesicular		38 (76%)
with Prolong Expiration		
Bilateral Creptitation		5 (10%)

Mean white blood cell (WBC) count was $12,603 \pm 5027$, lymphocytosis (>40%) in 84%, C- reactive protein (CRP) was negative in 64%. (Table- VI)

Table-VI: Investigations

Investigations	Frequency (%)	
WBC	Mean	$12,603 \pm 5027$
	<1500/cmm	37 (74%)
	>1500/cmm	13 (26%)
Neutrophil	Mean	34.7 ± 15.3
	<70%	49 (98%)
	>70%	1 (2%)
Lymphocyte	Mean	55.9 ± 13.2
	<40%	8 (16%)
	>40%	42 (84%)
CXR	Sticky Density	6 (12%)
	Patchy Opacity	3 (6%)
	Right Upper Lobe	2 (4%)
	Collapse Consolidation	
CRP	< 6	32 (64%)
	>6	16 (36%)

All children received 3% NaCL nebulization (100%), oxygen therapy (76%) and intravenous fluid (44%). (Table – VII)

Table- VII: Supportive Rx

Supportive Rx	Frequency (%)
Counselling	50 (100%)
Nebulized 3% NaCl	50 (100%)
Oxygen Therapy	38(76%)
Intravenous Fluid(IVF)	22(44%)
Chest Physiotherapy	2 (4%)

Table –VIII & IX showing mean duration (days) of outcome variables of our cases. Mean duration of return of social smile was 1.52 ± 1.58 , normal feeding 0.74 ± 1.12 , no fast breathing 3.10 ± 1.94 , normal SPO₂ > 90%/ mean duration of oxygen therapy 1.82 ± 1.39 and mean length of hospital stay 4.48 ± 1.78 .

Table –VIII: Outcome Variables

Outcome Variables	Mean Duration (Days)
Return of Social Smile	1.52 ± 1.58
No Feeding difficulty	0.74 ± 1.12
No Fast Breathing	3.10 ± 1.94
Normal SPO ₂ >90%	1.82 ± 1.39

Table –IX: Duration (Days)

Duration (Days)	Mean
Oxygen Therapy	1.82 ± 1.39
Length of the Hospital Stay (LOHS)	4.48 ± 1.78

Discussion:

Pharmacologic options for the treatment of bronchiolitis include oxygen (O₂) therapy; beta2-adrenergic agonists, racemic epinephrine; corticosteroids; ribavirin; antibiotics; and, recently, hypertonic saline.¹¹ Oxygen therapies acts as a direct bronchodilator and is indicated if oxygen saturations are less than 90% in order to avoid hypoxemia. Short-acting beta2-agonists dilate the bronchioles, improving oxygenation and breathing. Several systemic reviews showed that using bronchodilator may improve clinical symptom scores, however the effects are transient; they do not play role in disease resolution, the need for hospitalization, or length of stay. Additionally, use of these medications is associated with adverse effects, including tachycardia and tremors.^{14,15} As a result, the 2014 AAP guidelines no longer recommended using short acting beta2- agonists in infants and children with bronchiolitis without a reactive airway component.¹¹ Racemic epinephrine has its agonistic effects on alpha and beta receptors, helping to reduce edema and mucus plugging, however, its effects are transient, and studies as well as systematic reviews of the literature did not show a shortened

length of hospital stay.^{16,17} The use of corticosteroids in the treatment of bronchiolitis is controversial. A recent Cochrane systematic Review showed that use of corticosteroids was not associated with significant reductions in clinical scores, hospitalization rates, or length of hospital stay. However, recent literatures have focused on hypertonic saline for the treatment of bronchiolitis.¹⁸

Common trend in the management of bronchiolitis in our settings are use of oxygen, short acting beta-2 agonist and antibiotics as most physicians do not have enough confidence about not to use antibiotics in bronchiolitis. So, this study was conducted to evaluate the outcome of bronchiolitis using 3% NaCl nebulization with other supportive measures but without antibiotics. We selected few outcome variables which mainly helped us to take the decision of discharge such as return of social smile, no feeding difficulty, no fast breathing, normal oxygen saturation and length of hospital stay.

Between 1998 and 2014, 69 total articles were published evaluating hypertonic saline (HTS) effectiveness for bronchiolitis; 25 (36%) positive, 38 (55%) neutral, and 6 (9%) negative. However, between years 2010 and 2011, a total of 22 relevant articles were published, of which 7 were positive, 13 were neutral, and 2 were negative. Between years 2012 and 2014, 36 additional articles were published, of which 12 were positive, 20 were neutral, and 4 were negative. All of the negative studies in this period came in 2014.¹⁹

Kuzik et al showed that nebulized 3% hypertonic saline decreases LOHS 2.6 ± 1.9 days compared with 0.9% NaCl 3.5 ± 2.9 days.²⁰ However compared to our study LOH stay was little higher 4.48 days. On the contrary, Abdul et al did not find any advantage of 3% NaCl over 0.9% NaCl in terms of LOHS and clinical severity score.²¹ Sulbutamol with 0.9% NaCl nebulization is very popularly use treatment option in bronchiolitis in our country. Gupta et al mentioned that 3% NaCl is more effective and safe for non-asthmatic, moderately ill patients with acute bronchiolitis, reduced clinical severity scoring and LOHS compared to salbutamol with 0.9% NaCl.²² Joshua et al showed that median LOHS, of patients who received HTS was 3 days.¹⁹ In our study mean LOHS was 4.48.

The low rate of serious bacterial complications and secondary infections precludes the use of antibiotics. Treatment cost and bacterial resistance are two important concerns not to use antibiotics routinely in bronchiolitis.²³ A recent Cochrane systemic review did not find sufficient evidence to support the use of antibiotics for bronchiolitis.¹²

Kabir et al revealed that supportive therapy alone was found similar to those treated with combined supportive therapy and antibiotics (either oral or parenteral).²⁴ Comparison of the outcome variables between this study & a study done by Kabir et al titled "Management of Bronchiolitis Without Antibiotics: A multicenter Randomized Control Trial in Bangladesh" has shown in the following table—

Table of comparison

Outcome Variables	Improved on Specific Day	Present Study	Study by Kabir et al
No feeding Difficulty	On Day 4	100%	97.9%
No Fast Breathing	On Day 6	96%	95.8%
Normal SpO ₂ > 90%	On Day 2	88%	93.8%
Return of Social Smile	On Day 4	100%	95.8%

Limitations: This was an observational study, which complicates the evaluation of the treatment effectiveness of HTS. small sample size, clinical severity scoring was not done.

In 2014, the American Academy of Pediatrics (AAP) published updated guidelines on the diagnosis and management of bronchiolitis, which include new recommendations on the use of hypertonic saline. From the trials reviewed in this article, it was shown that, hypertonic saline has been very well tolerated. The concomitant administration of a bronchodilator may not be necessary to reduce feared adverse effects.¹

In conclusion, we agree with the AAP guideline (2014) regarding the use of nebulized hypertonic saline to reduce bronchiolitis scores and LOHS for infants with bronchiolitis who are expected to be hospitalized for more than 72 hours. Given the safety of this therapy and the lack of other effective therapies for these patients, use of hypertonic saline should be attempted in multiple doses in all patient care settings where nebulization can be administered.¹

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