Randomised Controlled Trial

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Comparison of nebulised 3% hypertonic saline with ipratropium bromide in treatment of children with bronchiolitis: a randomized control trial

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Introduction: Several drugs are in use for nebulization in children with acute bronchiolitis and no study has yet been conducted to compare the treatment outcome of nebulized ipratropium bromide and nebulized 3% hypertonic saline in Pakistan.
Objective: The objective was to compare the treatment outcome of nebulized hypertonic saline and ipratropium bromide in children with acute bronchiolitis.
Setting: Department of Pediatrics.
Study duration: October 2019 to March 2020.
Subjects and methods: A total of one hundred ($n = 100$) children of either sex diagnosed with acute bronchiolitis were enrolled and randomized either to be nebulized with 3% hypertonic saline or ipratropium bromide. Outcomes were assessed in terms of respiratory rate, heart rate, and SpO_2 and respiratory distress assessment instrument score at different time intervals, length of hospital stay, and need of admission.
Results: Respiratory rate and SPO_2 improved significantly at 60 min and 24 h, respiratory distress assessment instrument improved significantly at 30 min, 60 min, and 24 h after the treatment in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide. The length of hospital stay was significantly shorter (2.63 vs. 3.82 days, $P = 0.008$) and a lesser number of patients needed hospital admission (22% vs. 44%, $P = 0.019$) in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide.
Conclusions: Nebulization with 3% hypertonic saline resulted in significant improvement in symptoms, a shorter duration of hospital stay, and a lesser number of hospital admissions as compared to nebulization with ipratropium bromide in children with acute bronchiolitis.

Keywords: bronchiolitis, hypertonic saline, ipratropium bromide

Introduction

Acute respiratory syncytial viral bronchiolitis is the most common cause of lower respiratory tract infection in children younger than 2 years of age[1]. The recently discovered human metapneumo-virus (associated with around 5–7% of the total pneumonia admissions), bocavirus, and other viruses[2]. Lower respiratory tract infections are the leading infectious cause of death globally in children younger than 5 years[3]. The most frequently used medication for infants admitted with bronchiolitis was salbutamol (25.5%) according to a recent retrospective study[4]. Since many years different treatment modalities have been in practice but there has not been consensus on the use of a specific effective treatment[5]. Clinical practice guidelines of 2006 do not recommend the routine use of any medication for bronchiolitis[6].

Bronchiolitis features accumulation of cellular debris, profound edema of the submucosa and adventitia, increased mucus secretion, and peribronchiolar

mononuclear infiltration ultimately resulting in alveolar cell death[7,8]. Symptoms appear 10–24 h after infection in the form

HIGHLIGHTS

- This study shows that nebulization with 3% hypertonic saline resulted in a significant improvement in symptoms.
- It can lead to a shorter duration of hospital stay and a lesser number of hospital admissions as compared to nebulization with ipratropium bromide in children with acute bronchiolitis.

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of tachypnea, wheeze, respiratory distress, cough, vomiting, feeding difficulties, rhinitis, or occasional cyanosis.

The American Academy of Pediatrics and the Canadian Pediatric Society both released revised guidelines for the evaluation and treatment of bronchiolitis in children younger than 2 years old in 2014. While neither set of guidelines recommends using nebulized hypertonic saline for infants with bronchiolitis in the emergency department, they do agree that 3% hypertonic saline may be beneficial for patients with a longer length of stay (greater than 3 days) in the hospital[7].

An initial study of 1981 suggested that the bronchodilator effect of ipratropium bromide on wheezy toddlers improved lung function in 40% of cases[9]. However, in a double-blind randomized trial held (1983), no clinical benefit of nebulized ipratropium bromide was found in acute bronchiolitis[10]. A recent study has been done in Pakistan to compare the efficacy of ipratropium bromide (70.1%) with epinephrine (62.3%) and it has been concluded that both the drugs are equally effective in acute bronchiolitis in infant. The mean follows up respiratory distress assessment instrument (RDAI) score in patients receiving ipratropium bromide was 2.0 ± 0.7 while that in patients receiving nebulized epinephrine was 2.2 ± 0.6 ($P = 0.000$)[11].

Mohammad Ali Zamani concluded in a study in Iran that the mean ± SD length of recovery was 4.14 ± 0.9 and 3.06 ± 0.6 in the Ventolin (Salbutamol) and hypersaline groups, respectively. The mean ± SD RDAI criterion on the days two, three, four, and five, respectively, 5.68 ± 1.3, 4.85 ± 1.6, 3.62 ± 1.6, and 1.42 ± 0.8 in the Ventolin (Salbutamol) group and 4.25 ± 1.5, 3.2 ± 1.5, 2.54 ± 1.6, and 0.9 ± 0.54 in the hypersaline group; the mean RDAI criterion was significantly lower in the hypersaline 3% group ($P < 0.001$)[12]. Multiple studies have shown hypertonic saline to be safe and effective to improve clinical scores

in both outpatient and inpatient settings[13–16].

To date, ipratropium bromide is the most commonly used nebulized drug in Pakistan for the treatment of children with acute bronchiolitis and no study has been yet conducted to compare the treatment outcome of nebulized ipratropium bromide and nebulized 3% hypertonic saline in Pakistan. Hence, the present study will determine the treatment outcome of 3% hypertonic saline in the treatment of acute bronchiolitis in comparison with ipratropium bromide. Western researches have shown the effectiveness of 3% hypertonic saline, which besides being a cost-effective treatment modality, will also reduce the hospital stay of children with acute bronchiolitis in Pakistan.

Ipratropium bromide is a physiologically active anticholinergic that is used to treat children with bronchiolitis. Nebulized ipratropium bromide's effectiveness has been investigated in several multicenter trials, and its treatment has been found to be helpful. Nevertheless, there are few studies on the effectiveness of nebulized ipratropium bromide in Pakistani newborns. Nebulized ipratropium will be compared with a well-researched bronchodilator, nebulized epinephrine, in this trial to determine its efficacy. If effective, it will be added to a ward strategy for the treatment of bronchiolitis.

We aimed to compare the treatment outcome of nebulized hypertonic saline and ipratropium bromide in children with acute bronchiolitis.

The rationale of this study is to compare two medicines used to treat bronchiolitis in the event of an emergency. The findings of this study will help in choosing the best medication to treat the disease's symptoms and offer information on local treatment.

Materials and methods

This randomized controlled trial was conducted in the department of pediatrics, from October 2019 to March 2020. A sample size of 100 patients was calculated using the WHO sample size calculator keeping population SD 1.14, level of significance 5%, and CI 95%. A consecutive nonprobability sampling technique was used.

Population, mean RDAI with 3% hypertonic saline group: 4.25[12]. Population mean RDAI with the ipratropium bromide group: 2.0[11].

Our study is fully compliant with the CONSORT 2010 guidelines[17] (Supplemental Digital Content 1, http://links.lww.com/MS9/A230). A complete CONSORT 2010 checklist (Supplemental Digital Content 1, http://links.lww.com/MS9/A230) has been provided as a supplementary file. UIN researchregistry8543[18] identifies our study in the Research Registry. Our research adheres to the principles outlined in the Helsinki Declaration.

Inclusion criteria

Children between 2 and 24 months of age and diagnosed as bronchiolitis (as mentioned in the operational definition) based on the history of coryza and/or fever followed by respiratory distress were included.

Exclusion criteria

Children with a history of two or more respiratory distresses or current progressive distress requiring mechanical ventilation, having family history of asthma, chronic pulmonary heart disease, or suspected heart disease. Patients having previous use of bronchodilator (within 4 h) and glucocorticoids (within 48 h) and those having tachycardia greater than 180/min or tachypnea greater than 100/min were excluded.

Data collection procedure

A total of 100 children were selected from the Outpatient Department of FGPC (Pediatrics) after permission from the ethical committee and fulfillment of inclusion and exclusion criteria. After a detailed history and clinical examination the diagnosis of bronchiolitis was confirmed. Informed consent was taken from the parents of all children and they were randomly allocated in either of the two groups by the lottery method, as shown in Figure 1. Group 1 received 3 m1 of nebulized 3% hypertonic saline while Group 2 received 0.5 ml for infants and l ml for children 12–24 months nebulized ipratropium bromide (250 ug/m1) in 3 ml normal saline for 5 mins each at 0, 30, and 60 min along with other supportive measures like hydration and oxygen if required and assessed in terms of improvement of symptoms. Randomization was by prospective cases being allotted serial numbers.

All the children were assessed in the beginning and after each nebulization for the initial three nebulization with special emphasis on heart rate (HR), respiratory rate (RR), RDAI score and oxygen saturation by pulse oximetry (Sp02). Patients were followed up after completion of 24 h to assess the status at that time. All the information was collected by the researcher herself to limit the collection bias and human errors on the predesigned proforma.

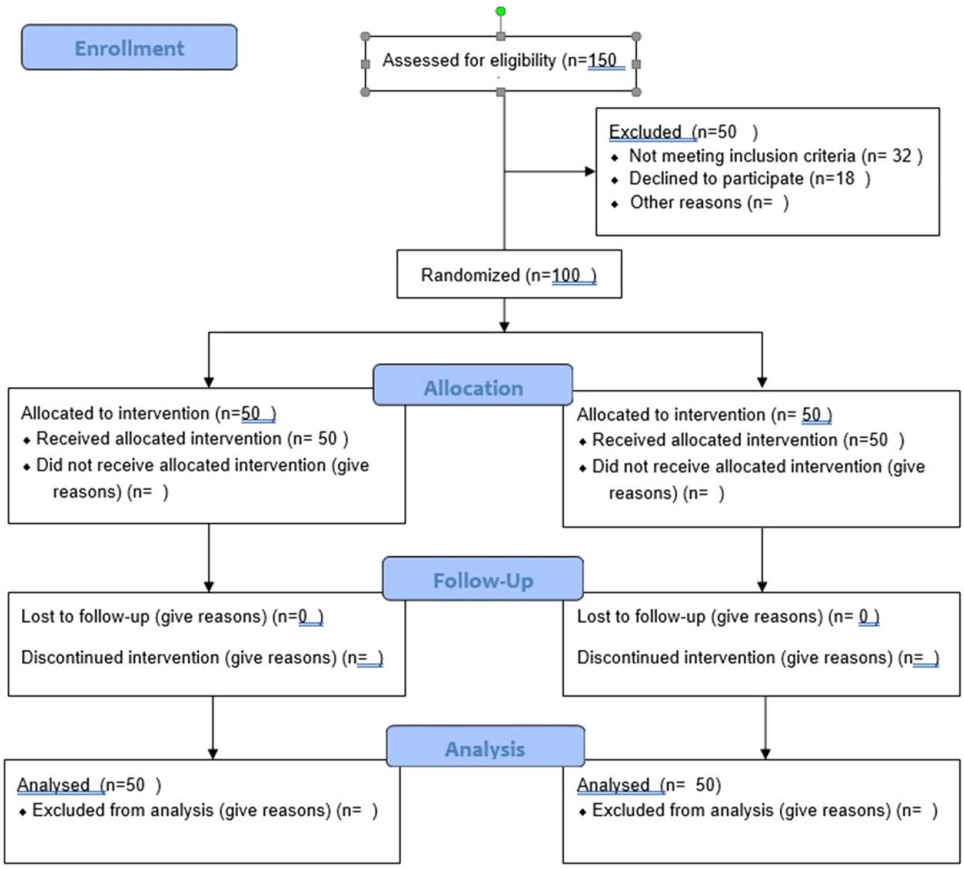

Figure 1. Consort flow diagram displaying the progress of all participants through the trial.

Data analysis procedure

The data was analyzed using SPSS version 24 for windows. Quantitative data like age, weight (Kg), fever (°F), RR (/min), HR (/min), RDA1, oxygen saturation, and length of hospital stay presented as mean ± SD.

Qualitative variables like sex were presented as frequency and percentage.

An independent sample *t*-test was applied to compare quantitative measures (e.g. RDAI) between two groups. Effect modifiers like sex and age were controlled through stratification. A poststratification independent sample *t*-test will be applied. A *P*-value ≤ 0.05 was considered as statistically significant.

Results

Demographic characteristics of enrolled subjects

In the present trial, a total of one hundred ($n = 100$) children of either sex diagnosed with acute bronchiolitis were enrolled. Patients were randomly divided into two groups I and II. Group 1 received 3 m1 of nebulized 3% hypertonic saline while Group II received 0.5 ml for infants and l ml for children 12–24 months nebulized ipratropium bromide (250 ug/m1) in 3 ml normal saline for 5 mins each at 0, 30, and 60 min along with other supportive measures like hydration and oxygen if required. The patient's condition was assessed in terms RR, HR, and SpO_2 and RDAI score. Sex and age distribution in each group described in Table 1.

Fever at 0, 30, 60 min, and 24 h after the treatment was not significantly different in both the treatment groups ($P > 0.05$ at all-time intervals. RR improved significantly at 60 min ($P = 0.020$) and 24 h ($P = 0.001$) after the treatment in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide. HR at 0, 30, 60 min, and 24 h after the treatment was not significantly different in both the treatment groups ($P > 0.05$ at all-time intervals. SPO_2 improved significantly at 60 min ($P = 0.008$) and 24 h ($P = 0.001$) after the treatment in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide. RDAI improved significantly at 30 min ($P = 0.005$), 60 min ($P = 0.005$), and 24 h ($P = 0.001$) after the treatment in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide (Tables 2 and 3).

Table 1

Distribution of sex in the study sample.

Sex	Group hypertonic ipratropium	Group saline bromide
Males	28 (56%)	32 (64%)
Females	22 (44%)	18 (36%)
Age		
2–12 Months	31 (62%)	25 (50.0%)
13–24 Months	19 (38%)	25 (50%)

Table 2

Fever, respiratory rate, heart rate, SPO2 and RDAI at different time intervals in patients who used hypertonic saline.

Time interval	Before nebulization		0 min		30 min		60 min		24 h	
Patients hypertonic saline	mean	P	mean	P	mean	P	mean	P	mean	P
Fever	99.68	0.325	99.58	0.483	98.72	0.892	98.26	0.298	98.04	0.562
Respiratory rate	62.08	0.529	61.72	0.314	58.20	0.056	54.30	0.020	49.80	0.001
Heart rate	138.42	0.313	138.14	0.336	140.68	0.704	143.14	0.686	145.94	0.850
SPO_2	90.24	0.684	90.32	0.294	92.06	0.131	93.42	0.008	95.60	0.001
RDAI	10.52	0.454	10.44	0.317	8.94	0.005	7.02	0.001	4.24	0.001

A similar trend was observed when the data was stratified for effect modifiers like age and sex (Tables 4–5).

Need of hospital admission and length of hospital stay

Lesser number of patients needed hospital admission (22 vs. 44%, $P = 0.019$, Table 6) and length of hospital stay was significantly shorter (2.63 days ± 1.12 SD vs. 3.82 days ± 1.06 SD, $P = 0.008$, Table 6) and in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide.

Lesser number of patients needed hospital admission who were nebulized with hypertonic saline (2.9 vs. 48%, $P = 0.04$) in 2–12 months. However, the length of hospital stay was similar for both groups. The need of hospital admission and length of hospital stay in both groups is shown in Table 7 was not significantly different in both groups at 13–24 months.

Males and females both needed greater admission when nebulized with ipratropium bromide. The length of hospital admission was not significantly different among both sex and both groups.

Discussion

Bronchiolitis is generally defined as a clinical syndrome of respiratory distress that occurs in children of less than 2 years of age. The characteristic features are upper respiratory symptoms that are followed by lower respiratory infection with inflammation resulting in wheezing or/and crackles. Treatment is mostly supportive as still there is no consensus on the single optimum treatment option. Our study results showed that RR and SPO_2 improved significantly at 60 min and 24 h, RDAI improved significantly at 30, 60 min, and 24 h after the treatment in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide. The length of hospital stay was significantly shorter (2.63 vs. 3.82 days, $P = 0.008$) and lesser number of patients needed hospital admission (22 vs. 44%, $P = 0.019$) in patients who were nebulized with hypertonic saline when compared to those nebulized with ipratropium bromide.

Table 4

Fever, respiratory rate, Heart rate, SPO_2, RDAI at different time intervals in hypertonic saline group. (Stratification).

	0 min		30 min		60 min		24 h	
	Mean	P	Mean	P	Mean	P	Mean	P
2–12 months								
Fever	99.7	0.586	98.7	0.889	98.3	0.310	98.0	0.698
RR	62.4	0.343	58.5	0.079	54.8	0.02	50.1	0.001
HR	138.4	0.290	141.4	0.101	143.8	0.876	146.4	0.789
RDAI	10.6	0.211	10.5	0.014	9.1	0.010	6.9	0.001
SpO2	90.3	0.392	92.1	0.140	93.4	0.006	95.7	0.001
13–24 months								
Fever	99.3	0.610	98.7	0.890	98.2	0.456	98.1	0.710
RR	60.6	0.357	57.7	0.081	53.4	0.020	49.3	0.001
HR	137.5	0.256	139.5	0.890	142.1	0.610	145.3	0.743
RDAI	10.4	0.456	10.3	0.234	8.8	0.011	7.1	0.001
SpO_2	90.4	0.311	92.2	0.123	93.5	0.110	95.4	0.010
Male								
Fever	99.6	0.781	98.7	0.891	98.3	0.981	98.0	0.981
RR	60.9	0.375	57.3	0.090	53.6	0.026	49.3	0.001
HR	138.1	0.810	140.6	0.670	143.1	0.121	145.5	0.640
RDAI	10.7	0.311	10.6	0.123	9.1	0.031	7.1	0.001
SpO_2	90.5	0.432	92.2	0.117	93.4	0.021	95.6	0.010
Female								
Fever	99.6	0.567	98.7	0.654	98.2	0.898	98.1	0.721
RR	62.7	0.368	59.3	0.101	55.2	0.029	50.5	0.001
HR	138.2	0.101	140.8	0.120	143.2	0.111	146.5	0.091
RDAI	10.3	0.765	10.3	0.431	8.8	0.032	7.1	0.001
SpO_2	90.1	0.561	91.9	0.890	93.4	0.031	95.6	0.010

Initial management of moderate to severe bronchiolitis centers on stabilization of respiratory and fluid status and determining the appropriate setting for continuation of care. We could not find any study in the literature comparing hypertonic saline and

Table 3

Fever, respiratory rate, heart rate SPO_2, and RDAI at different time intervals in patients who used ipratropium bromide.

Time interval	Before nebulization		0 min		30 min		60 min		24 h	
Patients Ipratropim bromide	mean	P	mean	P	mean	P	mean	P	mean	P
Fever	99.46	0.325	99.42	0.483	98.70	0.892	98.16	0.298	98.02	0.562
Respiratory rate	63.01	0.529	63.20	0.314	60.88	0.056	57.50	0.020	54.14	0.001
Heart rate	137.24	0.313	137.01	0.336	140.24	0.704	142.94	0.686	146.16	0.850
SPO_2	90.16	0.684	90.12	0.294	91.74	0.131	92.80	0.008	94.16	0.001
RDAI	10.74	0.454	10.73	0.317	9.92	0.005	8.36	0.001	6.60	0.001

Table 5

Fever, respiratory rate, Heart rate, SPO_2, RDAI at different time intervals in ipratropium bromide group. (stratification).

	0 min		30 min		60 min		24 h	
	Mean	P	Mean	P	Mean	P	Mean	P
2–12 months								
Fever	99.5	0.586	98.7	0.889	98.1	0.310	98.1	0.698
RR	63.4	0.343	61.2	0.079	58.1	0.02	54.6	0.001
HR	136.5	0.290	139.6	0.101	142.2	0.876	145.8	0.789
RDAI	11.1	0.211	11.1	0.014	10.1	0.010	8.5	0.001
SpO_2	90.1	0.392	91.4	0.140	92.5	0.006	94.1	0.001
13–24 months								
Fever	99.3	0.610	98.7	0.890	98.2	0.456	98.1	0.710
RR	62.9	0.357	60.5	0.081	56.9	0.020	53.7	0.001
HR	137.5	0.256	140.9	0.890	143.7	0.610	146.5	0.743
RDAI	10.5	0.456	10.5	0.234	9.8	0.011	8.2	0.001
SpO_2	90.2	0.311	91.8	0.123	93.1	0.110	94.2	0.010
Male								
Fever	99.5	0.781	98.8	0.891	98.2	0.981	98.1	0.981
RR	63.9	0.375	61.5	0.090	58.3	0.026	54.9	0.001
HR	138.3	0.810	141.4	0.670	144.1	0.121	147.4	0.640
RDAI	10.9	0.311	10.9	0.123	10.1	0.031	8.5	0.001
SpO_2	90.1	0.432	91.7	0.117	92.8	0.021	94.2	0.010
Female								
Fever	99.5	0.567	98.8	0.654	98.2	0.898	98.1	0.721
RR	62.1	0.368	59.8	0.101	56.1	0.029	52.7	0.001
HR	134.8	0.101	138.1	0.120	140.9	0.111	143.9	0.091
RDAI	10.4	0.765	10.4	0.431	9.6	0.032	8.2	0.001
SpO_2	90.3	0.561	91.9	0.890	92.9	0.031	94.1	0.010

ipratropium bromide in the treatment of infants and children with bronchiolitis. For infants and children with moderate to severe bronchiolitis, it is suggested not to routinely treat with nebulized hypertonic saline (of any concentration). In a 2018 meta-analysis of eight randomized trials evaluating administration of hypertonic saline in the ED, hypertonic saline reduced the rate of hospitalization among children with bronchiolitis (RR 0.77, 95% CI: 0.62–0.96), but there was substantial heterogeneity[19]. There are meta-analyses of randomized and quasi-randomized trials showed that nebulized hypertonic saline reduces length of stay (by approximately one-half day)[20,21]. Most of the trials included in the systematic reviews administered hypertonic saline with bronchodilators. However, a subsequent randomized, comparator-controlled trial found that, compared with normal saline, 3% hypertonic saline administered every 4 h without bronchodilators did not reduce length of stay in infants younger than 12 months of age who were hospitalized with bronchiolitis and had no significant comorbidities[22]. The 2015 NICE bronchiolitis guideline recommends against the use of

Table 6

Need of hospital admission and mean length of hospital stay.

		Hypertonic saline	Ipratropium bromide	P
Need of hospital admission	Yes	1122.0%	2244.0%	0.019
	No	3978.0%	2856.0%	
Mean length of hospital Stay	–	2.63 (±1.12 SD)	3.82 (1.06 SD)	0.008

Table 7

Need of hospital admission and Length of hospital stay in both groups (stratification).

	Hypertonic saline	Ipratropium bromide	P
2–12 Months			
Need of hospital admissions			
Yes	42.9%	1248.0%	0.004
No	2787.1%	1352.0%	
Length of hospital stay –	3.15	3.85	0.009
13–24 Months			
Need of hospital admissions			
Yes	736.8%	1040.0%	0.831
No	1263.2%	1560.0%	
Length of hospital stay –	2.14	3,80	0.001
Male			
Need of hospital admissions			
Yes	725.0%	1134.4%	0.429
No	2175.0%	2165.6%	
Length of hospital stay –	2.86	3.36	0.007
Female			
Need of hospital admissions			
Yes	418.2%	1161.1%	0.005
No	1881.8%	738.9%	
Length of hospital stay –	2.25	4.27	0.001

hypertonic saline in children with bronchiolitis[23]. The clinical practice guidelines of the American Academy of Pediatrics (AAP, 2014) recommend that bronchodilators not be used routinely in the management of bronchiolitis[6].

Routine administration of inhaled bronchodilators for children with bronchiolitis is not suggested. Meta-analyses of randomized trials and systematic reviews suggest that bronchodilators may provide modest short-term clinical improvement but do not affect overall outcome, may have adverse effects, and increase the cost of care[24,25]. For patients in whom such a trial is warranted, it is suggested to use albuterol 0.15 mg/kg (minimum 2.5 mg; maximum 5 mg) diluted in 2.5 to 3 ml normal (0.9%) saline and administered over 5–15 min or four to six puffs via a metered dose inhaler with spacer and face mask. Albuterol is preferable to epinephrine since albuterol is more appropriate for administration in the home setting. The effects should be monitored by evaluating the child before and up to one hour after treatment, recognizing that the clinician's ability to assess response may be limited[26]. If there is a clinical response to albuterol, it can be administered as needed (based on clinical status) every 4–6 h and discontinued when the signs and symptoms of respiratory distress improve.

Ipratropium bromide is thought to be synergistic with albuterol in therapy for acute childhood asthma. Despite widespread clinical use of its efficacy in bronchiolitis is uncertain. Schuh *et al.* in a double-blind, placebo-controlled trial enrolled 69 infants between 6 weeks and 24 months of age who exhibited the first episode of acute bronchiolitis and randomly assigned them to receive either nebulized albuterol (0.15 mg/kg per dose) and ipratropium bromide (250 micrograms per dose) (group A, $n = 36$) or nebulized albuterol and normal saline (placebo) (group B, $n = 33$) for two doses, 1 h apart. The two groups were comparable at baseline. Both therapies resulted in clinically significant improvement. However, the addition of ipratropium resulted in no additional benefit with respect to decrease in the RR (mean decreases 10.6/min vs. decreases 8.6/min, $P = .86$), accessory

muscle score (range 0 through 3) (decreases 0.92 vs. decreases 0.82, z = – 0.44), wheeze score (range 0 through 3) (decreases 0.94 vs. 0.85, z = – 0.20), oxygen saturation (increases 0.25% vs. increases – 0.33%, $P = .86$), or hospitalization rate (17 vs. 10)[27].

In another study, Bulent Karadag *et al.* investigated the efficacy of ipratropium bromide and salbutamol in the treatment of patients with moderate severe bronchiolitis. Patients were randomly assigned to receive nebulized salbutamol, ipratropium bromide, or placebo. The main outcome measures were changes in oxygen saturation rates and clinical scores and duration of hospitalization. In the bronchodilator groups, clinical scores were better compared to the placebo group at 30 min (8.4 +/- 1.3 vs. 7.5 +/- 0.8, $P < 0.05$). Bronchodilator groups also had significantly lower clinical scores (7.3 +/- 1.2 vs. 5.9 +/- 1.1, $P < 0.0001$, and 5.3 +/- 1.4 vs. 4.5 +/- 1.6, $P = 0.006$, respectively) and higher oxygen saturation rates compared to the placebo group at 8 and 24 h (89.6 +/-2.4 vs. 94.3 +/-4.4, and 92.2 +/-2.6 vs. 95.9 +/-4.4, respectively, $P < 0.0001$). Improvement rates and duration of hospitalization were not statistically different among groups[28].

In summary, we could not find any study in the literature comparing hypertonic saline and ipratropium bromide in the treatment of infants and children with bronchiolitis. However, the present study results and several other studies cited in the literature demonstrated that nebulized hypertonic saline has better efficacy than ipratropium bromide or other bronchodilators in terms of improvement in symptoms, shorter duration of hospital stay, and a lesser number of hospital admissions.

For infants and children with moderate to severe bronchiolitis, it is suggested not to routinely treat with nebulized hypertonic saline or bronchodilators. Nonetheless, if such a trial is warranted, hypertonic saline would be the better option. The present study has several strengths. The study was a randomized controlled trial and we followed stringent inclusion/exclusion criteria. Using a clinical score (RDAI) and RR as our primary outcome measures, we believe is another strength of the current study, as the RDAI is a noninvasive scoring instrument that may easily be adopted by clinicians in a nonstudy setting. The present study has several limitations.

Conclusion

Nebulization with 3% hypertonic saline resulted in significant improvement in symptoms, shorter duration of hospital stays, and a lesser number of hospital admissions. In several clinical experiments comparing the effects of different medications to saline, hypertonic saline has been utilized extensively as a 'placebo control'. Saline injections alone and in comparison to a variety of medication regimens have both been shown to have active analgesic effects.

Ethical approval

Ethical approval was granted by Federal Government Polyclinic Hospital, ref no FGH/ERC/Sep19/321.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

H.N.: study concept or design; S.M.: data collection; K.R. and A. T.: data analysis; N.N.: interpretation; I.H.: writing the paper; M.H. and H.M.: manuscript editing.

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