

Comparison of Hypertonic Saline vs Salbutamol in Normal Saline Nebulization in Children with Bronchiolitis

ANJUM ALI¹, HAFIZ MUHAMMAD MUAZ NAHEEM², ARSHAD RAFIQUE³, SIJJAD HUSSAIN⁴, MAKHDOOM RASHEED⁵, MUHAMMAD UZAIR⁶

¹MBBS FCPS Pediatrics, PGP (USA) Senior Registrar Pediatric Medicine, Central Park Medical College & Teaching Hospital, Lahore

²MBBS FCPS Pediatrics, Senior Registrar Pediatric Medicine, Central Park Medical College & Teaching Hospital Lahore

³MBBS FCPS Pediatrics, Associate Professor Pediatric Medicine, Central Park Medical College & Teaching Hospital, Lahore

⁴MBBS FCPS Pediatrics, Pediatrician Consultant, THQ Hospital, Chichawatni

⁵MBBS FCPS Pediatrics Senior Registrar Pediatric Medicine Central Park Medical College & Teaching Hospital, Lahore

⁶MBBS FCPS Pediatrics Assistant Professor Pediatric Medicine, Sahara Medical College, Narowal

Corresponding author: Anjum Ali, Email: miananjumali@gmail.com

ABSTRACT

Background: Main stay of treatment of acute Bronchiolitis is general supportive care, such as oxygenation, aspiration of respiratory tract secretions, and hydration therapy. Recent research indicates that breathed hypertonic saline is a potential treatment.

Objective: To compare the mean length of hospital stay and clinical bronchiolitis score of salbutamol nebulized in normal saline versus hypertonic saline in children with acute bronchiolitis.

Material and methods

Study Design: Randomized controlled design

Setting: Department of pediatrics, Fatima Memorial Hospital, Lahore.

Duration of Study: 6 months after approval of the study i.e. from 12th April 2017 to 12th October 2017.

Data Collection Procedure: Relevant parameters were identified, and the CBSS was computed. Using random tables, cases were divided among two groups and given salbutamol or hypertonic saline nebs. The length of stay was determined. The Clinical Bronchiolitis Severity Score (CBSS) was recorded based on various variables. Version 17 of the statistical package for social sciences was used for statistical analysis.

Result: Patients in the salbutamol group had a mean age of 13.56.66 months, while those in the hypertonic saline group had a mean age of 12.46.58 months. In the group receiving salbutamol, there were 29 males and 31 females. There were 32 men and 28 women in the hypertonic saline group. After 24 hours, the mean CBSS in the salbutamol group was 6.132.47, whereas in the hypertonic saline group, it was 4.881.75. After 24 hours of treatment, the difference in CBSS was significant between the two groups (P0.05). The mean duration of hospitalization was 3.920.81 days with salbutamol and 3.050.77 days with the hypertonic group. In both groups, there was a marked difference in duration of hospital stay (P0.05).

Conclusion: Thus, hypertonic saline was more effective than salbutamol in reducing the CBSS score and duration of hospital stay.

Keywords: Hospital Stay, Clinical Bronchiolitis Score, Nebulized Salbutamol, Normal Saline, Hypertonic Saline, Children, Acute Bronchiolitis.

INTRODUCTION

Acute bronchiolitis is the most common reason why infant and child with breathing difficulties end up in the hospital because they have an infection in their lower respiratory tract.^{1, 2} The risk of contracting this illness is highest in the first two years of life. Acute bronchiolitis shares many of the same symptoms with viral pneumonias, including a high temperature, wheezing, and rapid breathing. The ideal treatment for bronchiolitis is still unknown, despite the fact that it hospitalizes up to 2% to 3% of high-risk children per year (compared to only 1% of healthy infants).^{1, 3, 4}

Most cases of bronchiolitis are managed with supportive treatment, including oxygen administration, aspiration of respiratory tract secretions, and fluid management. In most cases, interventions are not found to have an impact on clinical severity, admission rate, or length of stay.^{1, 4, 5} Current clinical practice guidelines do not support the routine use of any medicine for bronchiolitis, however several other medical therapies are nevertheless often utilized anyway.^{1, 3}

Recent research indicates that breathed hypertonic saline is a potential treatment.

Obstruction of the small and medium airways can occur as a result of respiratory syncytial virus due to edema, necrosis, and sloughing of the respiratory epithelium. It is possible for hypertonic saline to drain fluid from submucosal and adventitial areas, hence reducing airway edema. The increased fluid content may loosen inspissated mucus and enhance muco-ciliary clearance. This discovery is pertinent for babies with bronchiolitis, who frequently have nasal obstruction symptoms. Inhibiting neutrophil CD11b/CD18 expression, elastase release, superoxide formation, and cytokine response, hypertonic saline could also have an immunomodulatory impact. The high cost of treating bronchiolitis is

directly related to the absence of effective treatments; hence, any therapy that might lessen the severity of the condition and enhance medical care could possibly result in major cost savings.^{1, 2}

Since 3% saline solution is known to be ineffectual for bronchiolitis, it is likely that the majority of the existing research on hypertonic saline solution in bronchiolitis are flawed.

In addition, various studies have utilized arbitrary endpoints, making it difficult to compare the trials.

93 infants with mild to moderate bronchiolitis were divided into two groups, with the control group receiving salbutamol dissolved in normal (0.9% saline) and the treatment group receiving salbutamol dissolved in hypertonic (3%) saline. They discovered that the remission period for wheezing was 3,8 + 1,1 days in the control group and 2,7 + 0,9 days in the treatment group (P 0.01). Wu S. et al. compared normal saline nebulization to hypertonic and discovered that the admission rate in the 3% hypertonic saline group was 28.9% compared to 42.6% in the normal saline nebulization group.

A recent randomized, double-blind experiment by Ipek IO split 120 newborns into four groups: group 1 got salbutamol and normal saline (NS), group 2 received salbutamol and hypertonic saline, and group 4 received NS. Patients' oxygen saturation and Clinical Bronchiolitis Severity Scores were tested before and after nebulizations, then again 48-72 hours later, and it was shown that both dramatically improved in all groups, with no significant differences between them. Post-treatment Ventolin CBSS (2.47 + 2.16) and hypertonic saline CBSS (2.27 + 2.07) were considerably higher than pre-treatment scores (4.87 + 1.01) and (5.03 + 1.27), respectively. However, there was no significant difference between groups.

This contradicts the findings of another study comparing salbutamol and hypertonic saline from Iran 7 in which the mean + SD length of recovery was 4.14 + 0.9 and 3.06 + 0.6 in the Ventolin and hypersaline groups, respectively, with a significantly shorter mean duration of recovery in the hypersaline group (p0.001).

Salbutamol is widely used in Pakistani hospitals to treat patients with bronchiolitis, despite the findings of several studies indicating that the drug is ineffective. Consequently, it is crucial to conduct research on this topic, as salbutamol is not supported by local evidence. Regarding the well-known side effects of salbutamol, the most common drug used to treat bronchiolitis, such as tachycardia, which limits its use, and higher costs compared to hypertonic saline, and the fact that no study has yet been conducted to compare the efficacy of salbutamol and hypertonic saline 3% on bronchiolitis in Pakistan, the present study will be conducted to determine the efficacy of hypertonic saline in inhibiting neutrophil CD11b/CD18 expression, elastase release, superoxide production, and cytokine response, hypertonic saline may also exert an immunomodulatory effect. The study will be a valuable contribution because it will help determine the efficacy of the two treatments, thereby reducing the disease's burden.

MATERIAL AND METHODS

Study Design: Randomized controlled design

Setting: Department of pediatrics, Fatima Memorial Hospital, Lahore.

Duration of Study: 6 months after approval of study, from 12th April 2017 to 12th October 2017.

Sample Size: Calculated sample size of 120 cases (60 cases in each group) is based on a 95% confidence interval, 80% test power, and expected mean length of hospital stay of 4.14 + 0.91 for the Ventolin group and 3.14 + 0.62 for the HS group.

Sampling Technique: Non probability consecutive sampling

Sample Selection

Inclusion Criteria: Children of both gender aged 1 month to 2 years with acute bronchiolitis as per operational definition and a CBSS of 4-8 on admission.

Exclusion Criteria: Saturation of oxygen should be less than 85% at room air.

Chronic cardiac diseases determined from medical record and history/examination.

Preterm birth or low birth weight <2500 g determined from medical record.

Previous episodes of wheezing or inhaled bronchiolitis use determined from medical record and history/examination.

Data Collection Procedure: A total of 120 infants aged 1 month to 2 years with bronchiolitis according to the operational criteria were chosen. After obtaining parental consent, a thorough medical history and physical examination are conducted. The entry of biodata into a predesigned structured performa. Relevant parameters were identified, and the CBSS was computed. Using random tables, cases were divided into two groups and given either salbutamol (0.15 mg/kg salbutamol) or hypertonic saline nebs. In addition to calculating the length of stay for each infant, pre- and post-treatment Clinical Bronchiolitis Severity Score (CBSS) variables such as respiratory rate, wheezing, retraction, and general condition at 24 hours were recorded. For ethical clearance, I submitted a synopsis to the committee on ethics.

Data Analysis Procedure: Version 17 of the statistical package for social sciences was used for statistical analysis. The gender information was reported as frequencies and percentages. Age and CBSS score quantitative data were presented as means and standard deviations. Using an independent sample t test, both groups' mean duration of hospital stay and CBSS scores were compared. A P value 0.05 was regarded as statistically important. For effect modifiers, data were stratified by age, gender, and CBSS score at presentation. A post-stratification t-test was conducted with a significance threshold of P 0.05.

RESULTS

Patients in the salbutamol group had a mean age of 13.56.66 months, whereas those in the hypertonic saline group had a mean age of 12.46.58 months. Table 1 shows that there were 29 males and 31 females in the salbutamol group. There were 32 men and 28 women in the hypertonic saline group. Fig 1

At the time of presentation, the mean CBSS was 9.751.53 in the salbutamol group and 9.431.66 in the hypertonic group. In both groups, there was no difference in CBSS at baseline (P>0.05). After 24 hours of treatment, 30 respiratory rate was observed in 15 (25.0%) children treated with salbutamol and 25 (41.7%) children treated with hypertonic saline; respiratory rate 30-45bpm was observed in 19 (31.7%) children treated with salbutamol and 23 (38.3%) children treated with hypertonic saline; 45-60bpm were observed in 10 (16.7%) children treated with salbutamol and 5 (8.3%) children treated with hypertonic saline. Significant difference was observed (P0.05). After 24 hours of therapy, no wheezing was noted in 11 (18.3%) children receiving salbutamol and 11 (18.3%) children receiving hypertonic saline (Table 3). Terminal expiratory only with stethoscope was observed in 12 (20%) with salbutamol and in 21 (35.0%) with hypertonic saline; Salbutamol induced full expiration or audible wheezing on expiration in 20 (33.3%) and hypertonic saline induced it in 17 (28.3%); salbutamol induced full inspiration and expiration in 17 (28.3%) and in 11 (18) (P>0.05). After 24 hours of therapy, no refraction was detected in 16 (26.7%) of the salbutamol-treated children and 21 (35%) of the hypertonic saline-treated children (Table 4). Intercostal only was observed in 13 (21.7%) with salbutamol and 20 (33.3%) with hypertonic saline. Tracheosternal were observed in 12 (20%) with salbutamol and 10 (16.7%) with hypertonic saline. (P>0.05) The difference was negligible. Normal condition was found in 32 (53.3%) children treated with salbutamol and 32 (53.3%) children treated with hypertonic saline after 24 hours of therapy (Table 5). Irritability, lethargy, and poor feeding were observed in 28 (46.7%) animals treated with salbutamol and 28 (46.7%) animals treated with hypertonic saline. (P>0.05) The difference was negligible. After 24 hours, the mean CBSS in the salbutamol group was 6.132.47 while it was 4.882.04 in the hypertonic saline group. After 24 hours of therapy, the difference in CBSS was significant among the two groups (P0.05). The mean hospital duration was 3.920.81 days for the salbutamol group and 3.050.77 days for the hypertonic group (Table 7). In both groups, there was a significant difference in length of hospital stay (P0.05). Table 8 contains data stratified by the age of the children. The mean CBSS for children aged 1 to 12 months was 9.951.29 with salbutamol and 9.411.70 with hypertonic saline. In both groups, the difference was insignificant (P>0.05). The mean CBSS was 9.631.65 with salbutamol and 9.461.57 with hypertonic saline in children aged 13-24 months. In both groups, the difference was insignificant (P>0.05). Table 9 was stratified according to the age of children. In children aged 1 to 12 months, the mean hospital stay with salbutamol was 4.050.84 days compared to 3.000.80 days with hypertonic saline. In both groups, the difference was significant (P0.05). In children aged 13 to 24 months, the mean hospital stay with salbutamol was 3.840.79 days compared to 3.110.74 days with hypertonic saline. In both groups, the difference was significant (P0.05). Table 10 was stratified according to the gender of children. The mean CBSS for male children was 9.831.56 with salbutamol and 9.471.74 with hypertonic saline. In both groups, the difference was small (P>0.05). The mean CBSS for female children was 9.681.51 with salbutamol and 9.391.65 with hypertonic saline. In both groups, the difference was small (P>0.05). Table 11 was stratified according to the gender of children. The mean hospital stay for male children was 3.830.71 days with salbutamol and 2.940.80 days with hypertonic saline. In both groups, the difference was significant (P0.05). In female children, the mean length of hospitalization with salbutamol was 4.000.89 days compared to 3.180.72 days with hypertonic saline. In both groups, the difference was significant (P0.05). Table 12 contains stratified baseline CBSS data. After 24 hours, the mean CBSS for children with a CBSS of 7-9 was

8.300.61 with salbutamol and 8.060.88 with hypertonic saline. In both groups, the difference was small ($P>0.05$). The mean CBSS for children with a CBSS of 10-12 was 10.940.86 with salbutamol and 11.000.77 with hypertonic saline. In both groups, the difference was small ($P>0.05$). Table 13 contains stratified baseline CBSS data. The mean hospital stay for children with CBSS 7-9 was 3.850.82 days with salbutamol and 3.190.79 days with hypertonic saline. In both groups, the difference was significant ($P0.05$). In children with CBSS 10-12, the mean length of hospitalization with salbutamol was 3.970.81 days compared to 2.840.74 days with hypertonic saline. In both groups, the difference was significant ($P0.05$). Table 14

Table 1: Descriptive statistics of age of patients

		Group	
		Salbutamol	Hypertonic Saline
Age (months)	n	60	60
	Mean	13.5	12.4
	SD	6.66	6.58
	Minimum	1	1
	Maximum	24	24

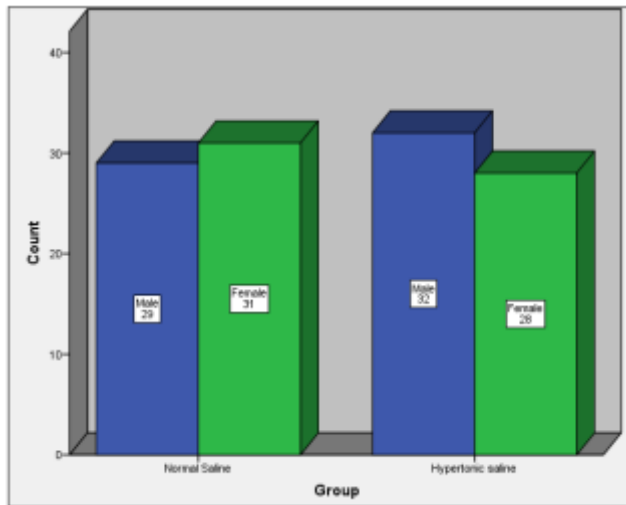


Fig. 1: Distribution of gender of patients

Table 2: Comparison of CBSS at time of presentation in both groups

		Group	
		Salbutamol	Hypertonic Saline
CBSS at baseline	n	60	60
	Mean	9.75	9.43
	SD	1.53	1.67
	Minimum	7	7
	Maximum	12	12

Independent sample t-test = 1.084, p-value = 0.280 (Insignificant)

Table 3: Comparison of respiratory rate in both groups

		Group		Total
		Salbutamol	Hypertonic saline	
Respiratory rate	<30	15 (25.0%)	25 (41.7%)	40 (33.3%)
	30-45	19 (31.7%)	23 (38.3%)	42 (35.0%)
	45-60	10 (16.7%)	5 (8.3%)	15 (12.5%)
	>60	16 (26.7%)	7 (11.7%)	23 (19.2%)
Total		60 (100%)	60 (100%)	120 (100%)

Chi-square test = 8.069, p-value = 0.045 (Significant)

Table 4: Comparison of wheezing in both groups

		Group		Total
		Salbutamol	Hypertonic saline	
Wheezing	None	11 (18.3%)	11 (18.3%)	22 (18.3%)
	Terminal expiratory or only with stethoscope	12 (20.0%)	21 (35.0%)	33 (27.5%)

	Expiration audible throughout or audible on expiration without a stethoscope	20 (33.3%)	17 (28.3%)	37 (30.8%)
	Inspiration and expiration without stethoscope	17 (28.3%)	11 (18.3%)	28 (23.3%)
Total		60 (100%)	60 (100%)	120 (100%)

Chi-square test = 3.984, p-value = 0.263 (Insignificant)

Table 5: Comparison of refraction in both groups

		Group		Total
		Salbutamol	Hypertonic saline	
Refraction	None	16 (26.7%)	21 (35.0%)	37 (30.8%)
	Intercostal only	13 (21.7%)	20 (33.3%)	33 (27.5%)
	Tracheosternal	12 (20.0%)	10 (16.7%)	22 (18.3%)
	Severe with nasal flaring	19 (31.7%)	9 (15.0%)	28 (23.3%)
Total		60 (100%)	60 (100%)	120 (100%)

Chi-square test = 5.914, p-value = 0.116 (Insignificant)

Table 6: Comparison of general condition in both groups

		Group		Total
		Salbutamol	Hypertonic saline	
General condition	Normal	32 (53.3%)	32 (53.3%)	64 (53.3%)
	Irritability, lethargy, poor feeding	28 (46.7%)	28 (46.7%)	56 (46.7%)
Total		60 (100%)	60 (100%)	120 (100%)

Chi-square test = 0.000, p-value = 0.999 (Insignificant)

Table 7: Comparison of CBSS after 24 hours in both groups

		Group	
		Salbutamol	Hypertonic Saline
CBSS	n	60	60
	Mean	6.13	4.88
	SD	2.47	2.04

Independent sample t-test = 3.023, p-value = 0.003 (Significant)

Table 8: Comparison of hospital stay in both groups

		Group	
		Salbutamol	Hypertonic Saline
Hospital stay	n	60	60
	Mean	3.92	3.05
	SD	0.81	0.77

Independent sample t-test = 6.017, p-value = 0.000 (Significant)

Table 9: Comparison of CBSS after 24 hours in both groups stratified for age

Age (months)	CBSS	Group		p-value
		Salbutamol	Hypertonic Saline	
1-12	n	22	32	0.207
	Mean	9.95	9.41	
	SD	1.29	1.70	
13-24	n	38	28	0.687
	Mean	9.63	9.46	
	SD	1.65	1.67	

Table 10: Comparison of hospital stay in both groups stratified for age

Age (months)	Hospital stay	Group		p-value
		Salbutamol	Hypertonic Saline	
1-12	n	22	32	0.000
	Mean	4.05	3.00	
	SD	0.84	0.80	
13-24	n	38	28	0.000
	Mean	3.84	3.11	
	SD	0.79	0.74	

Table 11: Comparison of CBSS after 24 hours in both groups stratified for gender

Gender	CBSS	Group		p-value
		Salbutamol	Hypertonic Saline	
Male	n	29	32	0.399

Female	Mean	9.83	9.47	0.491
	SD	1.56	1.72	
	n	31	28	
	Mean	9.68	9.39	
	SD	1.51	1.64	

Table 12: Comparison of hospital stay in both groups stratified for gender

Gender	Hospital stay	Group		p-value
		Salbutamol	Hypertonic Saline	
Male	n	29	32	0.000
	Mean	3.83	2.94	
	SD	0.71	0.80	
Female	n	31	28	0.000
	Mean	4.00	3.18	
	SD	0.89	0.72	

Table 13: Comparison of CBSS after 24 hours in both groups stratified for CBSS at baseline

CBSS at baseline	CBSS	Group		p-value
		Salbutamol	Hypertonic Saline	
7-9	n	27	32	0.219
	Mean	8.30	8.06	
	SD	0.61	0.80	
10-12	n	33	28	0.775
	Mean	10.94	11.00	
	SD	0.86	0.77	

Table 14: Comparison of hospital stay in both groups stratified for CBSS at baseline

CBSS at baseline	Hospital stay	Group		p-value
		Salbutamol	Hypertonic Saline	
7-9	n	27	32	0.002
	Mean	3.85	3.19	
	SD	0.82	0.78	
10-12	n	33	28	0.000
	Mean	3.97	2.89	
	SD	0.81	0.74	

DISCUSSION

In the United States, bronchiolitis, an infection of the lower respiratory system, is the primary cause of baby and child hospitalization. There are few therapeutic alternatives for the treatment of bronchiolitis. Numerous clinical investigations on the inhalation of hypertonic saline have had varied outcomes.

In our study, patients in the salbutamol group had a mean age of 13.56.66 months, whereas those in the hypertonic saline group had a mean age of 12.46.58 months. In the group receiving salbutamol, there were 29 males and 31 females. There were 32 men and 28 women in the hypertonic saline group. At the time of presentation, the mean CBSS was 9.751.53 in the salbutamol group and 9.431.66 in the hypertonic group. In both groups, there was no difference in CBSS at baseline ($P > 0.05$). After 24 hours, the mean CBSS in the salbutamol group was 6.132.47, whereas in the hypertonic saline group, it was 4.881.75. After 24 hours of therapy, the difference in CBSS was significant between the two groups ($P < 0.05$). The mean duration of hospitalization was 3.920.81 days with salbutamol and 3.050.77 days with the hypertonic group. In both groups, there was a significant difference in length of hospital stay ($P < 0.05$).

93 babies with mild to severe bronchiolitis were separated into two groups, with the control group getting salbutamol dissolved in normal (0.9% saline) and the treatment group receiving salbutamol dissolved in hypertonic (3%) saline. They discovered that the remission period for wheezing was 3,8 + 1,1 days in the control group and 2,7 + 0,9 days in the treatment group ($P < 0.01$). Wu S. et al. compared salbutamol nebulization to hypertonic saline and discovered that the admission rate in the 3% hypertonic saline group was 28.9%, compared to 42.6% in the normal saline group. According to Gupta et al., the CBSS scores for each group were 1,0 1,1 and 3,3 0,5, respectively ($P = 0.000$).

The average length of hospitalization was 3,4 1,7 days and 4,9 1,4 days, respectively ($P = 0.001$). Mandelberg et al. found that the average length of illness in the 0.9% saline group was 3.0 1.6 days and in the 3% hypertonic saline group it was 3.9 2.9 days. Tal et al. found that the average length of illness in the 0.9% saline group was 4.5 2.2 days and in the 3% hypertonic saline group it was 4.0 2.2 days. Kuzik et al. say that the 0.9% saline group had a survival rate of 4.0 2.4 days and the 3% hypertonic saline group had a survival rate of 4.5 2.3 days.

Mandelberg et al. found that people who got 3% hypertonic saline stayed in the hospital for an average of 3.1 days and people who got 0.9% saline stayed for an average of 4.1 days.

Tal et al. found that the average length of stay in the hospital was 2.6 1.4 days in the 3% hypertonic saline group and 3.5 1.7 days in the 0.9% saline group. Luo et al. found that the average length of stay in the hospital was 6.1.2 days in the 3% hypertonic saline group and 7.41.5 days in the 0.9% salbutamol group.

Group 1 got salbutamol and normal saline, group 2 received salbutamol and hypertonic saline, and group 4 received normal saline in a recent randomized, double-blind trial done by Ipek IO. The CBSS and oxygen saturation of patients were assessed before and after nebulizations, as well as 48-72 hours later, and it was observed that hospitalization rates (10%) and CBSS scores improved dramatically in all groups, with no significant differences. Post-treatment CBSS scores for Ventolin (2.47 + 2.16) and HS (2.27 + 2.06) improved significantly, although there was no difference between groups. In contrast to another study comparing salbutamol and HS from Iran in which the mean + SD length of recovery was 4.14 + 0.9 and 3.06 + 0.6 for the Ventolin and hypersaline groups, respectively, with a significantly shorter mean duration of recovery in the hypersaline group ($p < 0.001$).

In nine (75%) of the 12 most recent English-language randomized controlled trials evaluating the effect of salbutamol or albuterol on bronchiolitis, bronchodilators had no effect. In three of these studies, a difference was observed, but it resulted in a minor, transient improvement in the acute clinical score and had no effect on hospital admission rates or length of stay. In one of these three studies, ex-premature infants who may have had mild underlying chronic lung disease and whose response to bronchodilators may have been caused by this condition were not excluded. Several studies have reported that salbutamol or albuterol increases heart rate or decreases oxygen saturation. In four recent randomized controlled trials, the effect of ipratropium bromide (alone or in combination with salbutamol or albuterol) on bronchiolitis was evaluated, and none showed a significant effect.

CONCLUSION

Thus, hypertonic saline was more effective than salbutamol at reducing the CBSS score and length of hospital stay. Currently, we have local proof. Now and in the future, we will provide hypertonic solution to youngsters with acute bronchiolitis.

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