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Original Research Article

A comparative study of inhalational therapy versus supportive management in children aged 2 months to 2 years suffering from acute bronchiolitis

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ABSTRACT

Background: The study was conducted with the aim to compare the effectiveness of nebulized hypertonic (3%) saline and nebulized salbutamol over supportive management to assess and monitor the clinical response in the above three modalities of management, to compare the length of stay in the hospital and to identify the risk factors for severe disease.

Methods: This descriptive, cross-sectional hospital-based study was conducted at RICH Pediatric Hospital, Pogathota, Nellore, Andhra Pradesh from January 2015 to October 2016. A total of 120 children were included in the study. They were randomized into three treatment groups consisting of 40 in each. Group A received only supportive management, Group B received nebulization with 4 ml of 3% hypertonic saline along with supportive management and Group C received nebulization with 2.5 ml (2.5 mg) of salbutamol along with supportive management. Nebulization were given at intervals of 4 hours, six times a day until the patient was ready for discharge. Data was entered in Microsoft excel and analysis was done using SPSS version. A p-value of <0.05 was considered to be statistically significant.

Results: Out of 120 children involved in the study, majority 56 (46.66%) children were <6 months age. Male preponderance was observed in the study (M:F-1.4:1). Higher proportion of moderate to severe cases was from rural area (61 cases). More severe cases were seen in lower socioeconomic class people and who had history of second hand smoking (21.67%). Clinically better improvement was seen in children that received nebulized hypertonic saline along with supportive management with mean length of hospital stay of 2.5 days when compared to only supportive management with mean length of hospital stay of 3.25 days. The mean length of hospital stays with nebulized salbutamol along with supportive management is 3.05 days which is not clinically significant. Of the 120 children studied, 118 (98.33%) survived and were discharged, while 2 children who presented critically succumbed to death (1.67%).

Conclusions: Therapy with nebulized 3% hypertonic saline reduced the length of hospital stay in children <2 years suffering from acute bronchiolitis. Due to the efficacy and cost-effectiveness of the treatment, nebulized hypertonic saline should be considered for clinical management of acute bronchiolitis in children <2 years.

Keywords: Acute bronchiolitis, Inhalational therapy, Supportive management

INTRODUCTION

Acute bronchiolitis, is the spectrum of lower respiratory tract infections, and is a major cause of hospitalization in infants and children younger than 2 years of age.[1,2] Approximately 1 lakh bronchiolitis admissions occur annually in the United States at an estimated cost of $1.73 billion.[3] Acute bronchiolitis, usually is a self-limiting disease. Typically, illness begins with upper respiratory tract symptoms like nasal congestion and discharge, followed by lower respiratory tract symptoms and signs like persistent cough progressing to tachypnoea, wheeze, rales and use of accessory muscles. The disease peaks by 5-7 days and then gradually resolve. Most children who do not require hospitalization, recover by 28 days and those who require hospitalization, the average length of stay is 3-4 days.[4-6] The course may be prolonged in infants younger than six months and those with comorbid conditions.

The primary pathologic process in bronchiolitis includes airway and peribronchial inflammation, increased mucous production, sloughing of necrotic epithelial cells and impaired airway clearance. These process results in airway obstruction, gas trapping, atelectasis and impaired gas exchange.[7]

The standard treatment remains supportive care and includes nasal suctioning, supplemental oxygen, adequate feeding and fluid management. Despite the prominent role that inflammation plays in the pathogenesis of airway destruction, corticosteroids do not significantly reduce outpatient admissions when compared with placebo as per the recent Cochrane systematic review.[8]

The present study was conducted with the aim to compare the effectiveness of nebulized hypertonic (3%) saline and nebulized salbutamol over supportive management to assess and monitor the clinical response in the above three modalities of management, to compare the length of stay in the hospital and to identify the risk factors for severe disease.

METHODS

This descriptive, cross-sectional hospital-based study was conducted at RICH Pediatric Hospital, Pogathota, Nellore, Andhra Pradesh from January 2015 to October 2016. A total of 3856 children were admitted in the Pediatric ward with symptoms of bronchiolitis. Of these 168 children were clinically diagnosed as bronchiolitis. However, only 120 children were selected for the study based on the inclusion and exclusion criteria. The incidence of acute bronchiolitis was 4.35% of total Pediatric admissions.

Selection criteria

Children of 2 months to 2 years, presenting with a first episode of wheezing following a prodrome of upper respiratory tract symptoms along with signs of respiratory distress with no other explanation for wheezing were included in the study. Patients of age >2 years of age, previous episode of wheezing, prior use of oral or nebulized medications, pre-existing cardiac or pulmonary disease, immunodeficient, those with severe disease: SpO2 <88% on room air, RR >80/min, cyanosis, obtunded consciousness and progressive respiratory distress requiring mechanical ventilation and parents who refused to give informed consent were excluded from the study.

Sample size calculation

The parameter hospital stay is one of the important out-come and was considered for sample size calculation. The mean hospital stay for "Hypertonic (3%) Saline" treatment group is 4.8 (±1.2) days and the mean hospital stay for the "Salbutamol" treatment group is 6.4 (±1.4) days from the previous study with the difference d=1.6 days and expected population variance 1.695 days. At 99% of confidence interval Zα/2 = 2.576 and at 90% Power Zβ = 1.282.

$n = [\{(Z_{(\alpha/2)} + Z_{\beta})\}^2 \times 2 \times \sigma^2) / d^2$
$n = [\{(2.576 + 1.282)\}^2 \times 2\times (1.695)] / (1.6)^2$
$n = 19.71 \cong 20$

The minimum required sample size per group is 20. The overall sample size required is 60.

Grouping of patients

A total of 120 patients were randomized into three treatment groups consisting of 40 in each. Block randomization technique was used to maintain the equal sizes for all the treatment groups.

Patients were randomized to receive one of the three modalities of management i.e. Group A: only supportive management, Group B: nebulization with 4 ml of 3% hypertonic saline along with supportive management, Group C: nebulization with 2.5 ml (2.5 mg) of salbutamol along with supportive management. Nebulizations were given at intervals of 4 hours, six times a day until the patient was ready for discharge. Nebulizations were given using a conventional jet nebulizer with tight fitting face mask connected to a source of pressurized oxygen, set to a flow rate of 7 L/min. The nebulization was continued till the nebulization chamber was empty.

Patients were assessed and monitored for improvement or worsening of the condition, at admission and then at 12 hourly intervals using the clinical severity score described by Wang et al, (Table 1) until discharge.[9] Regarding the clinical total score, the disease severity is graded as mild (score 0-4), moderate (score 5-8), and severe (9-12). The length of stay in the hospital is considered from admission to time taken to reach clinical score of ≤3.

Statistical analysis

Data was entered in Microsoft excel and analysis was done using SPSS version. Significance was assessed at 5% level of significance. Categorical variables were compared using the Chi-square test and continuous variables were compared using One-way analysis of variance (ANOVA). The mean±SD expresses the central trend of data. A p-value of <0.05 was considered to be statistically significant.

Table 1: Clinical severity score.

Variables	Score			
	0	**1**	**2**	**3**
Respiratory rate				
<1 year	<50	51-60	61-70	>70
>1 year	<30	31-45	46-60	>60
Wheezing	None	Terminal expiratory or audible only with the stethoscope	Entire expiration or audible without stethoscope	Inspiration and expiration and audible without stethoscope
Retractions	None	Intercostal only	Trachiosternal	Severe with nasal flaring
General condition	Normal	-	-	Irritable, lethargy with poor feeding

RESULTS

A total of 3856 children were admitted in the Pediatric ward of RICH hospital Nellore, from January 2015 to October 2016. Of these 168 children were clinically diagnosed as bronchiolitis. However, only 120 children meet the requirements of the inclusion criteria and were included in the study. All the children were divided into 3 study groups by way of randomly allotted numbers. Each group consisted of 40 (33.33%) children and named as group A, B and C. Table 2 presents the distribution of patient's characteristics among different groups. Among these 56 (46.66%) children were <6 months age, 29 (24.16%) children were in 7-12 months, 21 (17.50%) were between 13-18 months and 14 (11.66%) were of 19-24 months age. The number and percentage of these patients randomized to A, B and C groups were given in Table 1. No clinical significance was noticed with respect to age in the 3 groups with p value of 0.999.

Table 2: Patients characteristics among three different groups.

Characteristics	Groups			Total	P value
	A	**B**	**C**		
Age (months)					
≤6	18 (32.14%)	19 (33.93%)	19 (33.93%)	56	0.999
7-12	10 (34.48%)	11 (37.93%)	8 (27.59%)	29	
13-18	7 (33.33%)	6 (28.57%)	8 (38.10%)	21	
19+	5 (35.71%)	4 (28.57%)	5 (35.71%)	14	
Sex					
Male child	24 (34.29%)	25 (35.71%)	21 (30.00%)	70	0.879
Female child	16 (32.00%)	15 (30.00%)	19 (38.00%)	50	
Socioeconomic status					
Low	18 (31.58%)	21 (36.84%)	18 (31.58%)	57	0.931
Middle	20 (34.48)	18 (31.03%)	20 (34.48%)	58	
High	2 (40.00%)	1 (20.00%)	2 (40.00%)	5	
Risk factors					
Secondary hand (SH) smoking	11 (27.50%)	8 (20.00%)	7 (17.50%)	-	0.528
History of allergy	5 (12.50%)	6 (15.00%)	5 (12.50%)	-	0.93
Locality					
Rural	19 (31.15%)	23 (37.70%)	19 (31.15%)	61	0.587
Urban	21 (35.59%)	17 (28.81%)	21 (35.59%)	59	

Among the three different groups (A, B, C) the number and percentages of males were 24 (34.29%), 25 (35.71%), 21 (30.00%) respectively and of females were 16 (32.00%), 15 (30.00%), 18 (38.00%) respectively. There was no clinical significance with respect to gender in the 3 groups with p value of 0.879.

57 children were of the low socioeconomic class, 58 children were of the middle socioeconomic class, 115 (95.83%) children belonged to the low and middle classes. 5 children were of high socioeconomic class. There was no clinical significance with respect to socioeconomic status in the three groups with p value of 0.931. Of the smokers, distribution in the 3 groups was Group A 11 (27.50%), Group B 8 (20%), and Group C 7 (17.5%) and no clinical significance with respect to second hand smoking and history of allergy was observed in the three groups with p values of 0.528 and 0.93 respectively. A total of 61 children were from rural area and 59 children were from urban area and no clinical significance with respect to locality was observed with p value of 0.587.

Table 3: Comparison of clinical severity score with patients' characteristics.

Patient characteristics	Clinical score severity at admission			Total	P value
	≤4 (mild)	5-8 (moderate)	9+ (severe)		
Socio economic status					
Low	7 (12.28%)	23 (40.35%)	27 (47.37%)	57	0.018
Middle	12 (20.69%)	30 (51.72%)	16 (27.59%)	58	
High	3 (60.00%)	2 (40.00%)	0 (0.00%)	5	
SH smoking					
Yes	2 (7.69%)	7 (26.92%)	17 (65.38%)	26	0.002
No	20 (21.28%)	48 (51.06%)	26 (27.66%)	94	
History of allergy					
Yes	3 (18.75%)	7 (43.75%)	6 (37.50%)	16	0.983
No	19 (18.27%)	48 (46.15%)	37 (35.58%)	104	
Locality					
Rural	6 (9.84%)	28 (45.90%)	27 (44.26%)	61	0.025
Urban	16 (27.12%)	27 (45.76%)	16 (27.12%)	59	

Table 3 provides the data regarding to the comparison of clinical severity with patients' characteristics. Children with moderate to severe clinical score belonged to low 23 (40.35%), 27 (47.37%) and middle 30 (51.72%), 16 (27.59%) SES respectively. Only 5 children were from high SES with 3 (60%) and 2 (40%) with mild and moderate score respectively. There was clinically significant difference among the different SES classes with p value of 0.018.

Out of 26 children exposed to smoking, 2 (7.69%) had mild, 7 (26.92%) had moderate and 17 (65.38%) had severe clinical score. Out of 94 children not exposed to smoking 20 (21.28%) had mild, 48 (51.06%) had moderate and 26 (27.66%) had severe clinical score. There was significant difference between SH smoking versus clinical severity score with p value of 0.002.

Of the16 children with history of allergy, 3 (18.75%) had mild, 7 (43.75%) had moderate and 6 (37.50%) had severe clinical score. Of the 104 children not having history of allergy, 19 (18.27%) had mild, 48 (46.15%) had moderate and 37 (35.58%) had severe clinical score. No significant difference was noticed with p value of 0.983.

Majority of children from rural area presented with moderate 28 (45.90%) and severe 27 (44.26%) severity. While there was no significant difference in urban children with 16 (27.12%) with mild, 27 (45.76%) with moderate and 16 (27.12%) with severe score. There was clinically significant difference between rural and urban children in terms of clinical severity of the disease with a p value of 0.025.

Table 4: Mean length of hospital stay among three different groups.

Groups	Length of stay		
	N	Mean	SD
A: Supportive management	40	3.25	0.87
B: Hypertonic (3%) saline	39	2.51	0.683
C: Salbutamol	39	3.05	0.686

Mean length of hospital stay between three groups were presented in Table 4. 40 children in Group A, received supportive management with a mean length of stay of 3.25 and SD of 0.87.

39 children in Group B received Hypertonic (3%) saline with a mean length of stay of 2.51 and SD of 0.683. 39

children in Group C received Salbutamol with a mean length of stay of 3.05 and SD of 0.683.

Clinically significant difference was noticed between three groups with respect to length of stay (p<0.01).

As shown in Table 5, there was clinically significant difference with supportive management vs. hypertonic (3%) saline in the 3 groups with a p value of 0.000 in terms of length of stay. There was clinically significant difference with hypertonic saline vs. salbutamol in the 3 groups with a p value of 0.002 in terms of length of stay.

Table 5: Mean, SE and P value between different groups.

Length of stay				
(I) Group	**(J) Group**	**Mean difference (I-J)**	**Std. error**	**Significance**
Supportive management	Hypertonoic (3%) saline	0.737	0.169	0.000
	Salbutamol	0.199	0.169	0.243
Hypertonoic (3%) Saline	Supportive management	-0.737	0.169	0.000
	Salbutamol	-0.538	0.170	0.002
Salbutamol	Supportive management	-0.199	0.169	0.243
	Hypertonoic (3%) saline	0.538	0.170	0.002

Table 6: Distribution of outcome.

Outcome	No. of Cases	Percentage
Survive	118	98.33
Death	2	1.67
Total	120	

Of the 120 children studied, 118 survived and were discharged, while 2 children who presented critically succumbed to death as shown in Table 6.

DISCUSSION

Acute bronchiolitis is a common clinical condition for which many children under 2 years of age are being admitted in the hospital. Though, it is a self-limiting condition, the morbidity lasts for several days. Cough takes two to three weeks to subside completely. Also, it is economic burden to the parents.

The present study was conducted in the RICH Hospital, from January 2015 to October 2016. Out of 168 children diagnosed clinically as bronchiolitis, 120 children were eligible for the study based on the inclusion and exclusion criteria. In the present study, these children were studied for risk factors for the development of disease and compared the response to nebulized hypertonic (3%) saline and nebulized salbutamol therapy to the supportive management, in terms of clinical severity improvement and overall length of stay in the hospital.

In this study, the incidence of bronchiolitis in less than 2 years is 4.35% and 3.06% in infants, of the total pediatric admissions in the hospital and the mortality is 1.67%. This was similar to the findings of Deshpande et al.[10] In another study by Bush et al the incidence in infants ranged from 2-3%.[11] In the present study, Increased incidence of bronchiolitis was noticed in the age group of 2 to 6 months (46.67%), followed by 7 to 12 months (24.17%) age. This was in accordance with the observations of Langley et al.[12] Male child were more affected than females (M:F-1.4:1). Similar observations were seen in the study of Shakil et al.[13]

Passive smoking is one of the environmental risk factor for the development of acute bronchiolitis.[14] Out of 120 cases, 26 (21.67%) cases had positive history of passive smoking. Of these 26 cases, 17 (65.38%) cases had clinical severity score of >9, 7 (26.9%) cases had scores of moderate severities at the time of presentation to the hospital. In the present study significant association was seen between SHS and acute bronchiolitis (p value 0.002). These observations were similar to the findings of Farzana et al.[15] A highly significant association was observed in their case study of 64 cases. Parental smoking carried 2.8 times risk of developing severe bronchiolitis.

In this study, most of the cases belong to lower to middle socioeconomic status. Out of 120 cases, 57 (47.50%) cases belong to low status, 58 (48.33%) cases belong to middle status and only 5 (4.17%) cases were of higher socioeconomic status. Similar findings were also seen in previous studies of Iqbal et al.[16]

In the present study, the response to the three modalities of management is assessed by the clinical severity score, and 12th hourly until discharge. The length of stay in the hospital is measured from the time of admission to reach clinical severity score of ≤3. The mean length of hospital stay in Group A was 3.25±0.87, in Group B it was 2.51±0.683 and Group C it is 3.05±0.686. There was clinically significant difference between the Groups A, B and C with respect to length of stay (p value of 0.01).

So, it is observed that, early improvement in clinical severity score and early discharge of cases before half to

one day was noticed in Group B cases receiving nebulization with hypertonic (3%) saline along with supportive management. Cases receiving nebulized salbutamol (Group C) along with supportive management is not so statistically significant as Group B. These findings were in accordance with the studies of Luo et al and Kuzik et al.[17,18]

Limitations of the study of this study were:

- A larger study cohort needed to generalize study findings more appropriately.
- Most of the children from lower socio-economic class attends the government hospital. The data from these cases could not be taken in the present study.
- Risk factors were identified by univariate analysis. The factors found to be significant on univariate analysis should have been subjected to multiple regression logistic analysis to evaluate independent factors of morbidity due to acute bronchiolitis.

CONCLUSION

The results of the study conclude that acute bronchiolitis is a common respiratory illness seen in children below 2 years of age with an annual incidence is 4.35% of total pediatric admissions during the months between November and February. Moderate to severe cases was noticed in rural areas, in lower socioeconomic class people and in those who had history of second hand smoking. Better improvement clinically was seen in children receiving 3% hypertonic saline nebulization along with supportive management with mean length of stay of 2.5 days when compared to only supportive management.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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