Original Article

Comparison of Nebulised 3% Hypertonic Saline with 0.9% Normal Saline for Treatment of Acute Bronchiolitis in Children up to 2 Years of Age

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Abstract

Background: Bronchiolitis is one of the most common lower respiratory tract infections in children and its incidence varies from country to country with studies reporting up to 18% of total admissions due to bronchiolitis with most of the cases occurring during winter. In our study we compare efficacy of nebulised 3% hypertonic saline with 0.9% normal saline for treatment of acute bronchiolitis in children up to 2 years of age in terms of mean days of hospital stay and clinical severity score.

Methods: This Randomized controlled trial (RCT) was done in department of Paediatrics, POF Hospital Wah Cantt from 1st November 2015 to 31st March 2016. Children in group 1 were nebulized with 3% hypertonic saline and group 2 with 0.9% normal saline.

Results: In group 1 the mean clinical severity score at the time of admission was 8.46 $\pm$ 1.10 and in group 2, 8.7 $\pm$ 0.98. In group 1 the mean clinical severity score after 3 days was 2.7 $\pm$ 0.87 and in group 2, 4.4 $\pm$ 0.999. The mean length of hospital stays for group 1 was 4.23 days $\pm$ 1.2 and in group 2 it was 6.4 days $\pm$ 1.4. Mean of clinical clarity score after 3 days and mean of length of hospital stay was compared between both groups for which the p value was significant.

Conclusion: Hypertonic saline (HS) nebulization has shown improved outcome in bronchiolitis. More studies are required to see the outcome of this method of treatment.

Key Words: Bronchiolitis, Hypertonic Saline, Normal Saline.

Introduction

Bronchiolitis is one of the most common lower respiratory tract infections in children and its incidence varies from country to country with studies reporting up to 18% of total admissions [1] due to bronchiolitis with most of the cases occurring during winter[2]. There is no consensus on definition of bronchiolitis but American Academy of Pediatrics (AAP) have defined it as "a constellation of clinical symptoms and signs including a viral upper respiratory prodrome followed by increased respiratory effort and wheezing in children less than 2 years of age" [3]. Respiratory syncytial virus (RSV) is the most common virus causing bronchiolitis [4] followed by Rhinovirus , human boca virus , human metapneumo virus, entero, adeno, corona and Influenza viruses [5, 6].

Clinically bronchiolitis presents with cough, rhinorrhea, fever, feeding problems, tachypnoea, wheezing and fine inspiratory crackles on auscultation [7, 8]. Optimal treatment of acute bronchiolitis is controversial and includes therapies like supportive care [9, 10], racemic adrenaline [11], salbutamol [12], nebulized normal saline, nebulized hypertonic saline [13] and corticosteroids [14]. Recent studies have shown beneficial effect of nebulization with 3% hypertonic saline (HS) as compared to 0.9 % normal saline (NS) nebulization [15].

Acute respiratory illness (ARI) is one of the leading causes of death in young children in Pakistan with around 30% of these deaths occurring under age 5 years [16]. Currently there is limited published data regarding use of 3% HS for the management of acute bronchiolitis in Pakistan. Thus this study was done to investigate the efficacy of nebulised 3% HS compared to 0.9% NS for the management of acute bronchiolitis in children under 2 years of age.

Material and Methods

This Randomized Control Trail (RCT) was done in department of Paediatrics, POF Hospital Wah Cantt over a period of six months from 1st November 2015 to 31st March 2016 after the approval of ethical committee of hospital. Sample size was calculated by using WHO formula with following values:

- Level of significant = 5%
- Power of test = 90%
- Population mean[15] = 2.4
- Anticipated mean[15] = 4.1
- Pooled standard deviation = 1

Required sample size was 30 children with acute bronchiolitis in each group. Non-Probability Sampling technique was used in this study.

Inclusion Criteria:

- All children aged up to 2 years with first episode of acute wheezing following upper respiratory tract infection with clinical severity score of 0-8 and SpO_2 < 94% at room air.

Exclusion Criteria:

- History of recurrent wheezing
- Congenital Heart Disease
- Severe Disease at presentation or respiratory failure
- Use of nebulized hypertonic saline within previous 12 hours
- Premature birth (gestational age ≤ 34 weeks)
- Radiological evidence of pneumonia including infiltrates / consolidation

Operational Definitions:

3% Hypertonic Saline

3% hypertonic saline contains 30 g/L of NaCl with ionic concentrations of Sodium and Chloride equal to 513 mEq/L, osmolarity of 1027 mOsmol/L and pH of 5.0 (4.5 to 7.0). 4 ml was given per dose in nebulised form.

0.9% Normal Saline:

Normal saline contains 9 g/L of NaCl with ionic concentrations of Sodium and Chloride equal to 154 mEq/L and pH of 5.0 (4.5 to 7.0). 4 ml was given per dose in nebulised form.

Clinical Severity Scores

The clinical score was calculated as shown [15] (Table 1):

Table 1: Clinical severity score:

VARIABLE	0 POINT	1 POINT	2 POINT	3 POINT
Respiratory Rate	< 30 breaths/min	31-45 breaths/min	breaths/min	>60 breaths /min
Wheezing	None	terminal expiratory or heard only with a stethoscope	entire expiration or audible on expiration without a stethoscope	inspiration and expiration without a stethoscope
Retractions	None	Intercostal only	Tracheosternal	Severe with nasal flaring.
General condition	Normal	Irritable	lethargic	Poor

feeding

The clinical total score ranks as:

- 0–4.9 points, mild;
- 5–8.9 points, moderate; and
- 9–12 points, severe disease

Data Collection Procedure: After taking informed consent from parents /guardians all children up to 2 years of age fulfilling the above-mentioned inclusion criteria with diagnosis of acute bronchiolitis were enrolled in the study. A computer-generated table of random numbers were used to randomize the enrolled children into two groups, as group 1 for 3% HS and group 2 for 0.9% NS. Demographic features such as age and gender were noted on a specially designed performa. Children in both groups, group 1 and 2, were subjected to chest X-ray. In group 1 nebulisation with 4ml of 3% HS was given every 2 hours for 3 doses, followed by every 4 hours for 5 doses, followed by every 6 hours until discharge. Group 2 received nebulisation with 4ml of 0.9% NS at similar intervals as HS.

Clinical severity scores were calculated at the time of admission (baseline) and then the final clinical severity scores were calculated on the 3rd day of admission. The total length of hospital stay was recorded from day of admission to day of discharge. All inhaled therapies were delivered to children from standard oxygen driven hospital nebuliser through a tight-fitting face mask. Discharge criteria was clinical severity scores of < 4 and $SpO_2 \geq 95\%$ at room air.

Data Analysis Procedure: The data was entered and analysed using SPSS version 18. For continuous variables such as age, length of hospital stays and clinical severity score, mean ± SD were calculated. Frequencies and percentages were measured for categorical variables such as gender. To compare mean clinical severity score and mean length of hospital stay between the two groups, 3% HS and 0.9% NS, independent two sample Student t test were used and p-values was obtained. P value ≤ 0.05 was considered as significant.

Result

Total of 60 patients were included in the study with each group comprising 30 patients. Mean age of the patients included in the study was 12.1 ± 4.97. Mean age in group 1 was 12.5 months with minimum age 4 months maximum 21 months and STD ± 4.9. In group 2 mean age was 11.8 months with minimum age 4 months maximum 22 months and STD ± 5.08. There was predominance of males in the study. Comparison of both the groups is shown in Table 2.

Table 2: Comparison of Clinical Information Of Groups

VARIABLES	GROUP 1 (HS GROUP) (n-30)	GROUP 2 NS GROUP (n-30)
SEX:		
Male	18 (60 %)	19 (63 %)
Female	10 (40 %)	11 (37 %)
CATEGORIES OF AGE:		
1 – 6 months	5 (16.6 %)	6 (20 %)
7 – 12 months	9 (30 %)	9 (30 %)
13 – 18 months	12 (40 %)	12 (40 %)
19 – 24 months	4 (13.3 %)	3 (10 %)
MEAN CLINICAL SEVERITY SCORE	8.46 ± 1.10	8.7 ± 0.98
CLINICAL CATEGORY		
Moderate	15 (50 %)	13 (43.3 %)
Severe	15 (50 %)	17 (56.6 %)

At the time of admission, minimum clinical severity score in group 1 was 6 whereas in group 2 it was 7. Maximum clinical scores were 10 and 11 in group 1 and group 2 respectively. After 3 days of treatment, minimum clinical severity in group 1 was 1 and maximum score was 5 whereas in group 2 minimum clinical score was 3 and maximum was 7. Comparison of both groups after treatment is shown in table 3.

Table 3: Comparison Of Groups After Treatment

VARIABLES	GROUP 1 (n-30)	Group 2 (n-30)	P value
MEAN CLINICAL SEVERITY SCORE	2.7 ± 0.87	4.4 ± .99	0.0001
MEAN LENGTH OF HOSPITAL STAY	4.23 ± .27	6.43 ± .43	0.0001

After 3 days of treatment, 28 (93 %) patients from group 1 and 17 (57%) patients from group 2 were classified as having mild clinical disease whereas 2 (7%) from group 1 and 13 (43%) from group 2 had moderate clinical disease.

Stratification of clinical severity score with respect to age category showed that in 1-6 months category; in group 1 mean score was 2.800 ± 0.447 while in group 2 mean score was 4.000 ± 0.632. P-value was 0.006. In 7-12 months category; group 1 had mean score of 3.00 ± 0.866 and group 2 had mean score of 4.333 ± 1.322. P-value was 0.022. In 13-18 months category mean score was 2.667 ± 1.073 in group 1 and 4.75 ± 0.866 in group 2. P-value was 0.001. In 19-24 months category; 2.25 ±

0.50 was mean score in group 1 and 3.67 ± 0.577 was mean score in group 2. P-value was 0.018. Stratification results of clinical severity score with respect to gender and clinical category at admission are shown in Table 4:

TABLE 4: Stratification of mean Clinical Severity Score after treatment

VARIABLE	MEAN CLINICAL SEVERITY SCORE GROUP 1	MEAN CLINICAL SEVERITY SCORE GROUP 2	p VALUE
GENDER:			
Male	3 ± 0.97	4.42 ± 1.12	0.0001
Female	2.33 ± 0.49	4.27 ± 0.78	0.0001
CLINICAL CATEGORY AT ADMISSION:			
Moderate	2.13 ± 0.51	3.61 ± 0.65	0.0001
Severe	3.33 ± 0.72	4.94 ± 0.82	0.0001

Stratification of length of hospital stay with respect to age category showed that in 1-6 months category; in group 1 mean length of hospital stay was 4.200 ± 0.836 while in group 2 mean length of hospital stay was 6.333 ± 1.032. P-value was 0.005. In 7-12 months, category; group 1 had mean length of hospital stay of 4.444 ± 1.509 and group 2 had mean length of hospital stay of 6.333 ± 2.000. P-value was 0.038. In 13-18 months, category mean length of hospital stay was 4.250 ± 1.484 in group 1 and 6.500 ± 1.314 in group 2, P-value was 0.0001. In 19-24 months, category 3.750 ± 0.500 was mean length of hospital stay in group 1 and 6.667 ± 1.154 was mean length of hospital stay in group 2. P-value was 0.006. Stratification results of length of hospital stay with respect to gender and clinical category at admission are shown in Table 5:

VARIABLE	MEAN LENGTH OF STAY GROUP 1	MEAN LENGTH OF STAY GROUP 2	P VALUE
GENDER:			
Male	4.56 ± 1.46	6.42 ± 1.46	0.0001
Female	3.75 ± 0.75	6.45 ± 1.43	0.0001
CLINICAL CATEGORY AT ADMISSION:			
Moderate	3.46 + 0.51	5.38 + 1.04	0.0001
Severe	5.00 + 1.36	7.23 + 1.14	0.0001

TABLE 5: Stratification of mean length of hospital stay after treatment

Discussion

Bronchiolitis is a common respiratory tract infection in children whose treatment is still controversial. Nebulizations with various saline compositions have been found to be an effective treatment in literature and in this study we compared hypertonic saline nebulization with normal saline nebulisations.

In our study, mean age was 12.1 ± 4.97 months which is high as compared to Ahmad [17] and had predominance of males which was also shown by local studies [16, 17] and a Nepalese study which was a double blind controlled trial with similar sample size and age group [18]. This male predominance may be due to gender specific immune response to RSV infection [19]. Baseline characters of both the groups were same in our study. Patients nebulized with hypertonic saline had early resolution of symptoms as compared to the other group. This effectiveness of hypertonic saline nebulization has also been found by Luo et al in their prospective, randomized, single centre, double-blind controlled study [15.] Ejaz et al [20] in their study had documented that HS nebulization had resulted in decrease of clinical severity score in lesser time as compared to NS nebulization which is also present in our study. Due to the effectiveness of HS nebulization, clinicians have used it in patients presenting in emergency department which have resulted in decrease in hospital admissions and early discharge from out- patient department resulting in decrease hospital burden [21, 22].On the contrary, Florin et al [23] in their study did not find improved outcome of HS nebulization in emergency settings. Our study did not measure this outcome but can be done in future trials. Effect of HS nebulization on length of hospital stay had been a topic of interest for various researchers. In our study, the hospital stay of the patients who received HS nebulization was significantly reduced as compared to those who received NS nebulization as also shown by Cochrane review [24].On other hand; Silver et al[25] in their study which was done in a tertiary care hospital and Brooks et al [26] in their meta-analysis were unable to find any statistical effect of nebulization on the stay of the patients suffering from acute bronchiolitis. Their inference may be because of the reason that these studies enrolled only children under 1 year of age and our sample included children up to 2 years of age.

Bronchiolitis is a common cause of respiratory illness requiring hospital admission in our setup. Ours was a well-designed randomized control trial with blinding maintained throughout the study period to minimize

the bias. A previously validated clinical criteria scoring was used to assess the clinical response. This study showed early improvement and less stay in hospital in patients treated with hypertonic saline which was also found in national and international studies thus proving to be a better treatment modality. There were few limitations of our study. It was a single centred study and also had a small sample size. Another limitation was that in clinical response we did not check for the relapse in these cases.

Conclusion

Bronchiolitis is one of common respiratory emergencies encountered in paediatric emergency. Different methods of treatment have been suggested throughout the world. Use of hypertonic saline in treatment of children has shown improved outcome in our study. More randomized multicentre control studies with larger sample size should be carried out to see the outcome of this method of treatment.

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