

Adrenaline Plus 3% NaCl vs. 3% NaCl by Nebulisation in Bronchiolitis in Children: A Prospective Randomized Study**Adithya Nikhileshwar B¹, Mamta Suthar², Jayendra Gohil³, Pranav PUNASANVALA⁴**¹Assistant Professor, Department of Pediatrics, Dhanalakshmi Srinivasan Medical College & Hospital, Perambalur, Tamilnadu²Senior Resident, GMERS Himmatnagar Medical College³Professor, GMERS Junagadh Medical College⁴Associate Professor, Department of Paediatrics, Government Medical College, Bhavnagar

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Conflict of interest: Nil

Abstract**Background:** Lower respiratory tract infection (LRTI) (inflammation of the airways/pulmonary tissue) in younger children needing hospitalization, due to viral or bacterial infection presents with fast breathing, chest retractions, and wheezing. Acute bronchiolitis is responsible for half of LRTI in children less than 2 years. Various bronchodilators have been used in the treatment. None have been found to be efficacious.**Aims and Objectives:** To compare nebulized 3% NaCl alone, with, nebulised adrenaline plus 3% NaCl, in the treatment of LRTI with special reference to bronchiolitis in terms of improvement in SpO₂, decrease in Heart rate, Respiratory rate, Respiratory Distress Assessment Instrument (RDAI)score [0-17 min-max] and duration of hospital stay in patients aged 1-24 months.**Methods:** Children in the age group of 1-24 months with LRTI, and/ or bronchiolitis with RDAI score from 0 to 15, admitted in the Pediatric ward, Sir T G Hospital, Bhavnagar from October 2018 to August 2019.**Results:** Out of 114 children enrolled, 57 received Adrenaline plus 3% NaCl nebulisation; 57 received 3% NaCl nebulisation. There was improvement in both the Groups in Heart Rate, Respiratory Rate, SPO₂, Respiratory distress Assessment Instrument score and duration of stay. There was no significant difference in these parameters between the two groups except improvement in SpO₂ in Adrenaline plus 3% NaCl nebulisation group.**Conclusion:** In the LRTI, including Bronchiolitis; nebulised adrenaline plus 3% NaCl, is not superior to 3% NaCl nebulisation alone, in the clinical improvement. The trial was registered at (CTRI) ctri.nic.in (CTRI/2018/10/016093)**Keywords:** Bronchiolitis, LRTI, Adrenaline, 3% NaCl, Nebulisation, RDAI score

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Introduction

Lower respiratory tract infection (LRTI). LRTI is infection below the level of the larynx and may be taken to include: Bronchiolitis, Bronchitis, pneumonia,

pleural effusion/ empyema. The presentation of these conditions depends on age, infecting organism and site of infection. Acute bronchiolitis is an acute

inflammation of the bronchioles caused by viral infection. In a child younger than 2 years of age, bronchiolitis refers to a clinical syndrome usually characterized by rapid respiration, chest retractions, and wheezing [1]. It is one of the major cause for hospital admissions of infants younger than 1 year of age; most commonly, it affects infants between 2 and 6 months [2]. The infant characteristically presents with a viral infection with rhinorrhea, cough, a low-grade fever and, within 1 or 2 days the symptoms are followed by onset of rapid respiration, chest retractions and wheezing. The infant can show irritability, poor feeding, and vomiting [3].

In very young or premature infants, however, the presentation of disease is atypical and has features of severe pneumonia [4]. Usually, infants older than 4 weeks develop the clinical syndrome of acute bronchiolitis [5]. Risk factor of acute bronchiolitis usually include low levels of antibodies in cord blood, gender, birth month, absence of or minimal breast feeding, crowded living conditions, being a twin or triplet, low socio-economic status, and cigarette smoking mothers [6-8].

More than 50% of cases of bronchiolitis are caused by Respiratory Syncytial Virus (RSV). Others include parainfluenza virus, adenovirus, mycoplasma, rhinovirus, human metapneumovirus and bocavirus [9,10]. Around 3% of all children are hospitalized with acute bronchiolitis in their first year of life [11]. Despite the high prevalence, little consensus exists on the optimal management of acute bronchiolitis. Though drugs like budesonide and montelukast are useful in children with Bronchial asthma [12] management in Bronchiolitis is mainly supportive.

Humidified oxygen is delivered via nasal cannula or into a head box; the concentration required is determined by pulse-oximetry. The infant is monitored for apnea. Nebulised bronchodilators, such as salbutamol or ipratropium, are used

often, though there is no evidence that bronchodilators have any role in the treatment. Breast feeding or Fluids need to be given [9]. Various other treatments like, other inhaled bronchodilators- adrenaline, inhaled and systemic steroids [13], aerosolised human DNAase, ribavirin, antibiotics, leukotriene receptor antagonists, heliox, immunoglobulins are used [14]. Many of these treatments in infants are still in controversy.

Hence the current study was undertaken to compare the efficacy of combination of nebulized adrenaline plus 3% NaCl, with nebulised 3% NaCl alone, in decreasing the respiratory distress and duration of hospital stay among children with LRTI with special reference to bronchiolitis.

Aims and Objectives

To study the effectiveness of combination of nebulized 3% NaCl plus adrenaline, in comparison with 3% NaCl nebulisation alone, in hospitalized children with Lower respiratory tract infection especially acute bronchiolitis with reference to changes in

- Heart rate,
- Respiratory rate,
- Respiratory distress assessment instrument(RDAI) score,
- Oxygen saturation
- Duration of hospital stay.

Materials and Methods

Study design

Source of data: Children from 4 weeks to 24 months with Lower respiratory tract infection especially acute bronchiolitis admitted to the Pediatrics Ward, Sir Takhtasinhji General Hospital, Bhavnagar, Guj, India.

Duration of the study: The study was conducted from October 2018 to August 2019.

Type of the study: Hospital based prospective interventional single blinded randomized controlled study.

Enrollment and randomization

Inclusion Criteria:

- All cases of bronchiolitis with a Respiratory Distress Assessment Instrument (RDAI) [14] score of 0 to 15 [on a scale of 0 (mild) to 17 (severe)].
- All Cases of Lower respiratory tract infection with positive chest x ray and septic screen with a Respiratory Distress Assessment Instrument (RDAI) [12] score of 0 to 15 [on a scale of 0 (mild) to 17 (severe)].

Exclusion Criteria:

The following children were excluded from the study

- Who had a previous episode of wheezing
- Children less than 4 weeks of age
- Who had a known chronic cardiopulmonary disease
- Who were immune-deficient
- Who presented with pulse > 200/min, respiratory rate > 80/min, SpO₂ < 94% despite oxygen therapy, RDAI score above 15 or profound lethargy/ altered sensorium /convulsions
- Who were preterm with corrected age of less than 4 weeks at presentation
- Whose parents had not given consent
- Who had received oral or inhaled corticosteroids during the preceding 2 weeks
- Who had received any inhaled drug therapy for the current disease

Total admission in our pediatric department per year is 2000 patients. The study was time bound for 10 months. Prevalence rate of Bronchiolitis is 3 percent and other lower respiratory tract infections are another 5 percent of our total admissions. So a Sample size of 150 was considered adequate. Applying exclusion criteria, we could get a sample size of 114.

Ethics approvals

The study was approved by Institutional Review Board (IRB no. 811/2018), Government Medical College, Bhavnagar (ECR/557/Inst/GJ/2014/RR-17, 13/12/2017). The Trial was prospectively registered with clinical trial registry of India (CTRI) ctri.nic.in (CTRI/2018/10/016093). Consent was obtained from the parents of all the children.

Diagnosis: Children with Lower Respiratory tract infection presented with symptoms like high grade fever, breathing difficulty, cough and signs of respiratory distress, intercostal muscle indrawing, pyrexia, crepitations and wheeze on Auscultation. Chest X-ray showed consolidation and collapse with air-bronchogram in lobar pneumonia or multiple, bilateral opacities in Bronchopneumonia, Meniscus sign in Pleural effusion, shifting of trachea in empyema or hydropneumothorax. Septic screening including Elevated Total and differential counts, C - reactive protein (CRP), Erythrocyte sedimentation rate (ESR).

Age specific values of heart rate and respiratory rate are given in Table 1. Infants with acute bronchiolitis had tachypnoea, mild to moderate hypoxia, and signs of respiratory distress, such as nasal flaring and respiratory muscle use. Physical examination showed wheezing, crackles, rhonchi and prolonged expiration. Other findings were conjunctivitis and acute rhinitis.

Abdominal distension was also present in some due to pulmonary hyperinflation. Diagnosis was mainly clinical, based on the presence of, nasal discharge, wheezy cough, fine inspiratory crackles and/or high pitched expiratory wheeze and hyperinflation on chest X ray.

Monitoring: Monitoring of the clinical status was done by the RDAI score, Heart rate, Respiratory rate at admission, 24 hours and 72 hours during the hospital stay

and at the time of discharge and by measuring the oxygen saturation with pulse-oximeter. RDAI score is mentioned in Table 2. Respiratory distress assessment instrument (RDAI) provides a score ranging from 0 to 17, with a higher score indicating more severe respiratory distress. A clinical score of <4 was considered as mild disease, a score between 4 and 8 as moderate disease any score more than 9 as severe disease. Scores > 15 was considered seriously ill and excluded.

Investigations: Chest X-ray, complete blood count.

Treatment: Supportive treatment like supplemental oxygen, maintenance of hydration, and antipyretics were given as required. Antibacterial was added to patients with lobar pneumonia and bronchopneumonia, those with septic screen positive, high grade fever and blood culture positive patients. Further each child in the study was grouped into one of the treatment groups:

Group 1: 3% NaCl plus adrenaline group: Nebulised 3% saline plus nebulised adrenaline.

Group 2: 3% NaCl group: Nebulised 3% NaCl.

Criteria to start additional treatment at any point of time were:

- Increase in RDAI score by 2 points above the admission score
- RDAI score >15
- SpO₂ < 94% despite oxygen therapy

The medication dosages: Nebulised adrenaline 2ml with 3% NaCl 2ml per treatment in first group and Nebulised 3% NaCl 4ml per treatment in 2nd group every eight hourly till clinical improvement or discharge, whichever is earlier.

Outcomes: Outcomes were measured in terms of improvement in oxygen saturation, clinical assessment including Heart Rate, Respiratory Rate, Respiratory Distress Assessment Instrument score at 24 and 72 hours, and at discharge and the duration of hospital stay. Allocation of

subjects is described in Flow chart (Figure 1).

Criteria for discharge:

- Improvement in RDAI score to <2.
- Adequate food intake
- Afebrile for past 24 hours without antipyretic measures

Statistical Analysis: Unpaired t-test, One way repeated measures ANOVA were used.

Results

The mean age of presentation in Group A was 9.54 weeks in which the mean age of Bronchiolitis patients was 8.45 months and the mean age of Other LRTI patients was 10.09 months. In Group B the mean age was 9.85 months in which the mean age of Bronchiolitis patients was 10.50 months and the mean age of Other LRTI patients was 9.53 months.

In Group A, out of 57 cases, 32 (56%) were males and 25 (44%) were females. In males, 15 (26%) were having Bronchiolitis and 16 (28%) were having Other LRTIs. In females, 10 (17.5%) were having Bronchiolitis and 16 (28%) were having Other LRTIs.

In Group B, 35 (61%) were males and 22(39%) were females. In males, 16 (28%) were having Bronchiolitis and 19 (33%) were having Other LRTIs. In females, 10 (17.5%) were having Bronchiolitis and 12 (21%) were having Other LRTIs.

In total, there were 66 (58%) males and 48 (42%) were females. This is showed in Table 3.

There was no significant difference in age and number of male and female patients and number of Bronchiolitis and other LRTI patients in both the groups. Clinical features were also similar in both the groups.

Mean respiratory rate and mean RDAI score at admission were not statistically significant whereas mean heart rate and

mean SpO₂ at admission between both the groups were statistically significant.

Table 4 show the Mean heart rate and Mean SpO₂ at admission.

Mean heart rate at 24 hours, 72 hours and at discharge decreased comparatively in both the groups. Mean respiratory rate at 24 hours, 72 hours and at discharge decreased comparatively in both the groups.

Mean SpO₂ at 24 hours, 72 hours and at discharge increased comparatively in both the groups. Mean RDAI score at 24 hours, 72 hours and at discharge decreased comparatively in both the groups

Table 5 shows the Mean heart rate, Mean respiratory rate, Mean SpO₂ and Mean RDAI score at Admission, 24 hours, 72 hours and at Discharge.

Mean duration of stay between both the groups and also between the bronchiolitis patients of both the groups were not clinically significant.

Amongst 57 candidates in Group A, 31 were given Antibiotics and 26 were not given Antibiotics. In Group B, 31 were given Antibiotics and 26 were not given Antibiotics. Five Bronchiolitis patients from group A, and three Bronchiolitis

patients from Group B were given Antibiotics.

This is explained in Table 6.

One way repeated measures ANOVA was used for statistical analysis which showed that Decrease in mean Heart rate, Mean respiratory rate, Mean RDAI scores between the two groups were not statistically significant but increase in mean SpO₂ between both the groups was statistically significant. In the bronchiolitis patients of both the groups, Decrease in mean Heart rate, Mean respiratory rate, Mean RDAI scores and increase in Mean SpO₂ were not statistically significant. This is explained in Table 7 and Table 8

To avoid the confounding effect of Antibiotics, Comparison was done between the Patients, who were not given Antibiotics in both the groups and especially between the Bronchiolitis patients of both the groups using One way Repeated Measures ANOVA. There was no statistically significant decrease in Mean Heart rate, Respiratory rate and RDAI scores or increase in Mean SpO₂ between both the groups. There was also no significant difference in the mean duration of stay between both the groups and also between the Bronchiolitis patients of both the groups.

Table 1: Age specific normal values to define Tachycardia and Tachypnea²⁷

Age group	Heart Rate (minute)	Respiratory Rate (minute)
0 day – 3 months	100-180	35-55
3-6 months	90-180	30-45
6-12 months	80-170	25-40
1-2 year	70-140	20-30

Table 2: Respiratory Distress Assessment Instrument (RDAI) Score¹⁴

Sign	0	1	2	3	4
Wheezing					
Expiration	None	End	½	¾	All
Inspiration	None	Part	All	-	-
Lung fields	None	<2/4	>3/4	-	-
Retractions					
Supraclavicular	None	Mild	Moderate	marked	-
Intercostal	None	Mild	Moderate	marked	-
Subcostal	None	Mild	Moderate	marked	-

Total	0				17
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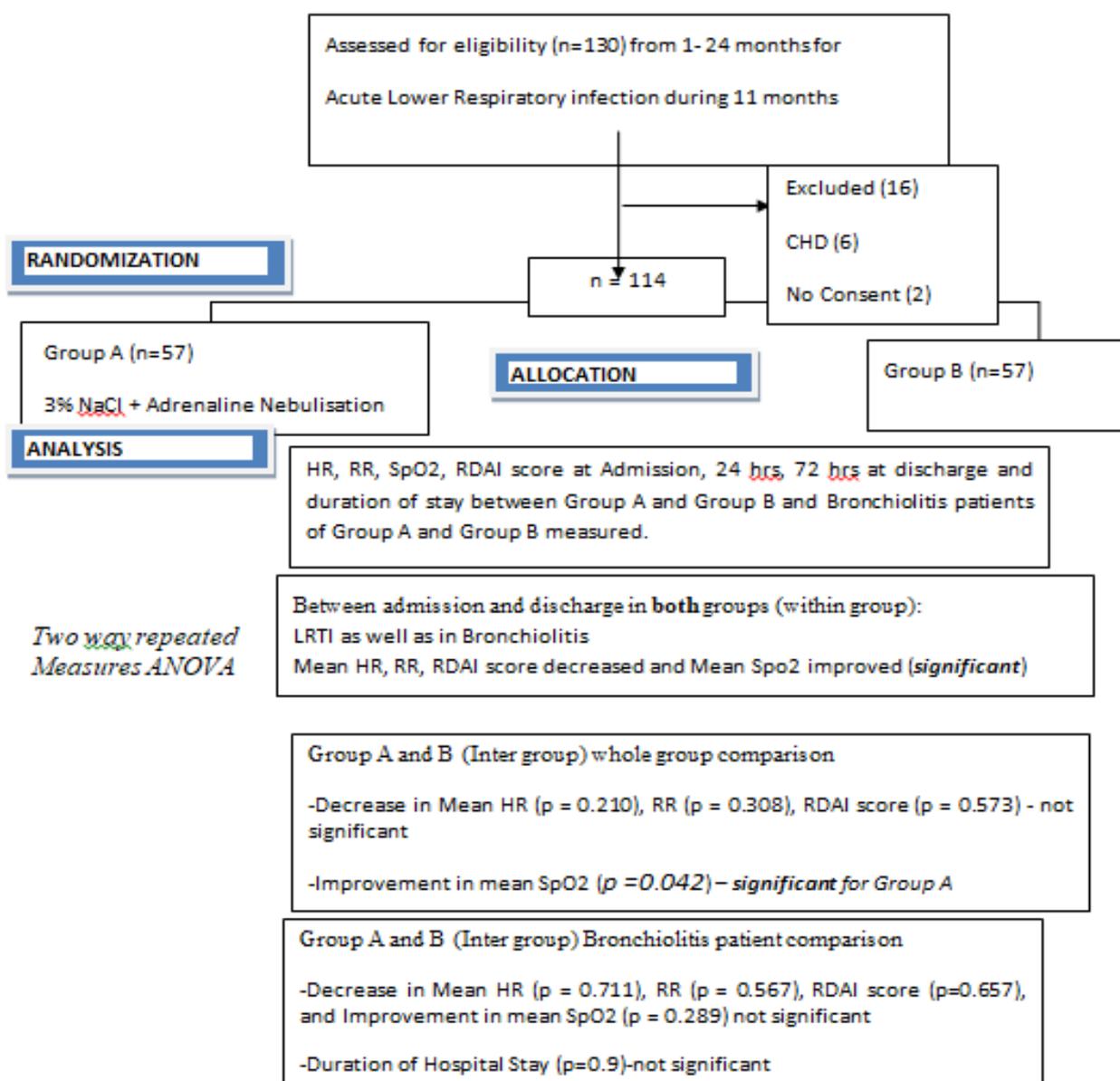


Figure 1: Flowchart

HR-Heart rate; RR- Respiratory rate; SpO₂- Oxygen saturation; RDAI-Respiratory distress assessment instrument; ANOVA- Analysis of variance; n-Total number; hrs-Hours; CHD- Congenital Heart Disease; Group A- Adrenaline plus 3% NaCl; Group B- 3% NaCl

Table 3: Distribution of Children According To Gender and Diagnosis

Group	Diagnosis	Gender		Total
		Male	Female	
A	Bronchiolitis	15	10	25
	Other LRTI	16	16	32
	Total	31	26	57
B	Bronchiolitis	16	10	26
	Other LRTI	19	12	31
	Total	35	22	57

(A+B) Total	66	48	114
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Table 4: Mean Heart Rate and Mean SpO₂ at admission

Group	Diagnosis	Mean HR/min (SD)	Mean RR/min (SD)	Mean SpO ₂ (SD)	Mean SpO ₂ (SD)
A	Bronchiolitis	118.71(15.98)	119(13.95)	96.71(1.50)	97.02(1.45)
	Other LRTI	120.81(12.30)		97.33(1.30)	
B	Bronchiolitis	116.66(20.13)	127(17.35)	96.41(1.44)	96.45(1.58)
	Other LRTI	129.21(15.31)		96.60(1.70)	
*p 0.007				*p 0.04	

Group A-Adrenaline plus 3% NaCl; Group B- 3% NaCl; LRTI- lower respiratory infection; HR-Heart rate; Min-Minute SD- Standard deviation.*p significant

Table 5: Comparison of Mean Heart Rate, Mean respiratory rate, Mean SpO₂, Mean RDAI score.

	Group	Diagnosis	Mean Heart Rate(SD)	Mean(SD)	Mean RR(SD)	Mean(SD)	Mean SpO ₂ (SD)	Mean(SD)	Mean RDAI score(SD)	Mean(SD)
Adm	A	Bronchiolitis	118.71 (15.98)	119.81 (13.94)	40.80 (9.27)	41.75 (9.55)	96.71 (1.50)	97.02 (1.45)	3.71 (1.16)	4.06 (1.35)
		other LRTI	120.81 (12.30)		42.70 (9.90)		97.33 (1.35)		4.42 (1.41)	
	B	Bronchiolitis	121.73 (20.13)	125.47 (17.35)	41.81 (13.80)	43.52 (11.85)	96.41 (1.44)	96.50 (1.58)	4.00 (1.35)	4.36 (1.64)
		other LRTI	129.21 (15.30)		45.23 (10.48)		96.60 (1.70)		4.73 (1.79)	
24 Hrs	A	Bronchiolitis	114.02 (13.64)	116.36 (12.95)	36.84 (9.27)	38.44 (8.56)	97.30 (1.50)	97.52 (1.18)	2.89 (1.16)	3.45 (1.59)
		other LRTI	118.21 (12.55)		40.05(9.01)		97.74 (1.19)		4.01 (1.61)	
	B	Bronchiolitis	115.03 (17.11)	120.52 (16.36)	38.72 (12.55)	41.15 (11.28)	97.11 (1.24)	96.99 (1.39)	3.31 (1.19)	3.99 (1.93)
		other LRTI	126.01 (14.89)		43.58 (10.11)		96.88 (1.52)		4.68 (2.21)	
72 Hrs	A	Bronchiolitis	108.4 (7.27)	109.90 (8.66)	33.37 (7.16)	34.53 (7.55)	97.92 (0.86)	98.08 (0.76)	1.10 (0.64)	1.30 (0.98)
		other LRTI	111.44 (9.56)		35.69 (7.94)		98.20 (0.65)		1.50 (1.09)	
	B	Bronchiolitis	08.37 (9.52)	111.08 (10.76)	35.72 (11.93)	38.11 (11.19)	97.85 (0.84)	97.83 (0.92)	1.35 (0.89)	1.63 (1.40)
		other LRTI	113.80 (12.58)		40.50 (10.51)		97.81 (0.97)		1.91 (1.66)	
Dis	A	Bronchiolitis	101.66 (5.68)	102.66 (6.45)	29.29 (5.68)	29.83 (5.35)	98.66 (0.64)	98.75 (0.55)	0.07 (0.27)	0.20 (0.43)
		other LRTI	103.67 (12.30)		30.37 (6.94)		98.84 (0.44)		0.34 (0.49)	
	B	Bronchiolitis	101.74 (8.07)	103.01 (7.18)	29.20 (8.70)	31.51 (6.13)	98.65 (0.62)	98.61 (0.70)	0.12 (0.32)	0.34 (0.49)
		other LRTI	104.28		33.82		98.57		0.56	

		(8.20)		(7.29)		(0.76)		(0.49)	
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Group A-Adrenaline plus 3% NaCl; Group B- 3% NaCl; HR- heart rate; RR-Respiratory rate;SpO2-Oxygen saturation; RDAI-respiratory distress assessment Instrument; SD- Standard deviation; Adm- Admission; Hrs- Hours; Dis-Discharge; LRTI- lower respiratory infection

Table 6: Mean Duration of Stay and Antibiotic usage

Group	Diagnosis	Mean SD duration of stay (days)	Mean (SD) duration of stay (days)	p value	Antibiotics Given	Antibiotics Not Given
A*	Bronchiolitis**	3.00 (1.13)	4.97 (2.49)	0.2*	5	26
	other LRTI	6.27 (2.65)			26	0
B*	Bronchiolitis**	4.23 (1.94)	5.54 (2.70)	0.9**	3	26
	other LRTI	6.86 (2.69)			28	0
Total					62	52
Antibiotics		A+B Bronchiolitis			8	52
		A+B other LRTI			54	0

Group A-Adrenaline plus 3% NaCl; Group B- 3% NaCl; LRTI- Lower respiratory tract infection

*Between Group A and Group B ** Between Bronchiolitis patients of Group A and Group B

Table 7: Statistical Analysis of data (Inter-Group Analysis)

One way Repeated Measures ANOVA Greenhouse-Geisser		Df	F	p value
Comparison of Group A and B	Mean Heart rate	1.814	1.583	0.210
	Mean Respiratory rate	1.691	1.165	0.308
	Mean SpO₂	1.755	3.373	0.042*
	Mean RDAI score	2.448	0.615	0.573
Comparison of Bronchiolitis in Group A and B	Mean Heart rate	1.502	0.255	0.711
	Mean Respiratory rate	1.304	0.430	0.567
	Mean SpO ₂	1.504	0.289	0.289
	Mean RDAI score	2.291	0.463	0.657

Group A-Adrenaline plus 3% NaCl; Group B-3% NaCl
df- Degree of Freedom, *Significant

Table 8: Statistical Analysis (Within Group Analysis Green House-geisser): parameters on admission, 24 hrs, 72hrs and at Discharge

ANOVA (within group)	p value (<0.05- Significant)			
	Heart rate	Respiratory rate	SpO ₂	RDAI score
Group A	0.000	0.000	0.000	0.000
Group A Bronchiolitis	0.000	0.001	0.000	0.000
Group B	0.000	0.000	0.000	0.000
Group B Bronchiolitis	0.000	0.017	0.000	0.000

Group A-Adrenaline plus 3% NaCl; Group B-3% NaCl

Discussion

In our study, both the groups showed improvement in parameters like Heart rate, Respiratory rate, Spo2 and RDAI scores. But the difference between both the group

overall and Bronchiolitis patients alone, were not statistically significant. The reason may be due to less frequent use of nebulisations in both the groups as more

frequent use of Adrenaline nebulisation could have shown significant clinical improvement.

The mean age of presentation in Group A was 9.54 months and group B was 9.85 months Parrott [5] showed that the incidence of bronchiolitis was high among the children < 1 year. Similar results were demonstrated by Jartti [15] and Chattopadhyaya [16].

In our study, 59% were males and 41 % were females. The results were similar to the previous studies conducted by Nagayama [17] and Boezen [18], which showed an increased susceptibility of bronchiolitis in male children. Although Boezen stated that the possible reason for this could be due to the immunosuppressive effect of the male hormones [18], however it does not seem to be true that, male hormones are active in infancy or that they are immunosuppressive.

In our study cold and rhinorrhoea was the most common presenting complaint seen in 106 (93%), followed by cough in 105 (92%). These observations were similar to Kellner JD *et al* [19] in which cough and fast breathing were the prominent symptoms. Fever was present in 74% in our study, however, El-Radhi *et al* [20] showed that fever in acute bronchiolitis was in 31% and that the children with fever in bronchiolitis had more severe disease course and longer duration of hospital stay (4.2 days vs 2.7 days). Infants who required mechanical ventilation were classified as very severe, those who required oxygen supplement as severe, and those who required admission for observation without oxygen requirement as mild. This was not found in our study because, though 74% patients had fever, they had mild and moderate course of disease only based on RDAI score.

Though there is significant improvement individually, our study has not demonstrated any statistically significant clinical improvement with Adrenaline plus

3% NaCl nebulisation combined when compared to 3% NaCl nebulisation alone. This was similar with results of Bahadily [21] prospective study on 100 infants by comparing the 3% NaCl or hypertonic saline and 0.9% normal saline nebulization in acute bronchiolitis.

The mean duration of hospital stay in the group of children treated with 3% hypertonic saline was shorter (4.7 ± 1.9 days). A Cochrane review of seven trials involving 581 infants (282 inpatients, 65 outpatients and 234 emergency department patients) with acute bronchiolitis found that nebulisation with 3% saline results in a significantly shorter length of hospital stay as well as a lower clinical score as compared to nebulisation with 0.9% saline [22]. Another Cochrane review concludes that inhaled (racemic) adrenaline does not improve important clinical outcomes such as length of hospital stay or the use of supportive care in moderate to severe bronchiolitis inpatients when compared to placebo [23]. This is supported by a large Norwegian randomised controlled trial (RCT) of 404 infants [24]. This finding is in accordance with our study. In a study conducted by Luo Z [25], it was found that there was no significant improvement in duration of hospital stay in patients who were given adrenaline nebulisation when compared with placebo. Similar results were observed by Abul-Ainine [26] in a study comparing the short term effects of nebulised adrenaline and saline placebo in infants with moderately severe acute bronchiolitis.

In our study, we found no adverse events like tachycardia related to the usage of Adrenaline plus 3% NaCl for nebulisation. In six of the seven trials of the Cochrane review [22,27], patients received hypertonic saline inhalation in conjunction with bronchodilators and no significant adverse events related to 3% saline inhalation were reported.

Conclusion

Both the groups reduced the respiratory distress and hence showed clinical

improvement. Thus Adrenaline plus 3% NaCl nebulisation and 3% NaCl nebulisation caused significant clinical improvement

However, there was no significant difference in the clinical improvement between the two groups. Thus the efficacy of Adrenaline plus 3% NaCl nebulisation is not superior to 3% NaCl nebulisation alone, when used in Lower respiratory tract infection especially Bronchiolitis.

Hence 3% NaCl nebulisation can be the initial choice for clinical improvement in bronchiolitis.

3% NaCl nebulisation can also be used as supportive treatment in other LRTI patients for symptomatic improvement.

There was no complication or adverse effects observed during the usage of either the Adrenaline plus 3% NaCl or 3% NaCl alone.

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References

1. Wohl MEB. Kendig's Disorders of the Respiratory Tract in Children. 7/e. Philadelphia: Saunders; 2006:432-46.
2. Henderson FW, Clyde Jr WA, Collier AM et al, The etiologic and epidemiologic spectrum of bronchiolitis in pediatric practice. J Pediatr. 1979; 95:35-9.
3. Mallory MD, Shay DK, Garrett J, Bordley WC. Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. Pediatrics. 2003; 111:e45-51.
4. Hall CB, Kopelman AE, Douglas Jr RG et al, Neonatal respiratory syncytial virus infection. N Engl J Med. 1979; 300:393-6.
5. Parrott Rh, Kim Hw, Arrobio Jo et al, Epidemiology of respiratory syncytial virus infection in Washington, DC: II. Infection and disease with respect to age, immunologic status, race and sex. Am J Epidemiol. 1973; 98:289-300.
6. Glezen WP, Paredes A, Allison JE et al, Risk of respiratory syncytial virus infection for infants from low-income families in relationship to age, sex, ethnic group, and maternal antibody level. Jpediatr. 1981; 98:708-15.
7. Spencer N, Logan S, Scholey S, Gentle S. Deprivation and bronchiolitis. Archdis child. 1996; 74:50-52.
8. Jansson L, Nilsson P, Olsson M. Socioeconomic environmental factors and hospitalization for acute bronchiolitis during infancy. Acta Paediatr. 2002;91:335-8.
9. Rudolph CD, Rudolph AM, Hostetter MK, Lister G, Siegel NJ. Pediatrics. 21/e2003:716-721.
10. Zorc JJ, Hall CB. Bronchiolitis: recent evidence on diagnosis and management. Pediatrics. 2010; 125:342-9.
11. Scottish Intercollegiate Guidelines Network. Bronchiolitis in children: a national clinical guideline. Scottish Intercollegiate Guidelines Network; 2006.
12. Shah MB, Gohil J, Khapekar. S, et al. Montelukast's budesonide as a first line preventive therapy in mild persistent asthma in 2-18 y. Indian J Pediatr2014;81:655-9.
13. Gohil JR, Sheladiya AM, Adithya NB, Bhojak RD. Adrenaline and dexamethasone, vs adrenaline and fluticasone, vs adrenaline alone in bronchiolitis: a randomized controlled trial. Asian J Pediatr Res.2020;3(1):20-8.
14. Carvalho WBD, Johnston C, Fonseca MCM. Bronchiolitis in Roger's Textbook of Intensive Care. 4/ed. Philadelphia: Wolters Kluwer Lippincott Williams & Wilkins. 2008: 716-721.
15. Jartti T, Lehtinen P, Vuorinen T, Ruuskanen O. Bronchiolitis: age and previous wheezing episodes linked to

- viral etiology and atopic characteristics. *Pediatr infect dis J*. 2009; 28:311-7.
16. Chattopadhyaya D, Chatterjee R, Anand VK et al, Lower respiratory tract infection in hospitalized children due to respiratory syncytial (RS) virus during a suspected epidemic period of RS virus in Delhi. *J Trop Pediatr*. 1992; 38:68-73.
 17. Nagayama Y, Tsubaki T, Nakayama S et al, Gender analysis in acute bronchiolitis due to respiratory syncytial virus. *Pediatr Allergy Immunol*. 2006;17:29-36
 18. Boezen HM, Jansen DF, Postma DS. Sex and gender differences in lung development and their clinical significance. *Clin Chest Med*. 2004; 25:237-45.
 19. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Efficacy of bronchodilator therapy in bronchiolitis: a meta-analysis. *Arch Pediatr Adolesc Med*. 1996; 150:1166-72.
 20. El-Radhi AS, Barry W, Patel S. Association of fever and severe clinical course in bronchiolitis. *Arch Dis Child*. 1999; 81:231-4.
 21. Al-bahadily AK, Al-Omrani AA, Atiya AA. Hypertonic 3% saline compared to 0.9%(normal)saline in treatment of acute bronchiolitis. *IntJPediatr*. 2017; 5(1):4209-16.
 22. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database Syst Rev*. 2017; (12):CD006458
 23. Hartling L, Bialy LM, Vandermeer et al. Epinephrine for bronchiolitis. *Cochrane Database Syst Rev*. 2011; 15:CD003123.
 24. Øymar K, Skjerven HO, Mikalsen IB. Acute bronchiolitis in infants, a review. *Scand J Trauma Resusc Emerg Med*. 2014; 22:23.
 25. Luo Z, Liu E, Luo J et al, Nebulised hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. *Pediatr Int*. 2010; 52:199-202.
 26. Abul-Ainine A, Luyt D. Short term effects of adrenaline in bronchiolitis: a randomised controlled trial. *Arch Dis Child*. 2002;86:276-9.
 27. Lawley LP, Siegfried E, Todd JL. Propranolol treatment for hemangioma of infancy: risks and recommendations. *Pediatr Dermatol*. 2009;26:610-4.