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# A Comparative study to assess the efficacy of Nebulised 3% hypertonic saline and Nebulised l-adrenaline in treatment of acute bronchiolitis in children 1 month to 2 years

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## Abstract

**Background:** Acute bronchiolitis is one of the most common respiratory illnesses affecting children in the age group 1 month to 2 years[1]. The etiology is almost always viral with respiratory syncytial virus(RSV), parainfluenza , influenza responsible for vast majority of cases[2]. The therapeutic options in the past have been humidified oxygen, inhaled bronchodilators and inhaled or oral corticosteroids. The response to these options was very variable among patients[3]. More recent interventions are heliox, hypertonic saline and nebulised L-adrenaline. Many previous studies have been conducted regarding the effects of these treatment options as well as their comparative efficacy among each other. Recently the role of nebulised 3% saline has come into focus, its efficacy being proven above other modalities in various studies[4]. Nebulised adrenaline has also been suggested as treatment option[5], its primary role being reduction of mucosal edema, which is an important part of the disease pathology in bronchiolitis. Hence L-adrenaline in nebulised form can be a potential therapeutic option in acute bronchiolitis.

**Objectives:** To compare the efficacy of nebulised 3% saline and nebulised L-adrenaline in treatment of acute bronchiolitis in children 1month to 2years of age. Other objectives were to observe any difference in the duration of hospital stay and duration of illness using each of these treatment options.

**Methods:** This prospective study was conducted on 100 children admitted with acute bronchiolitis in the department of Pediatrics, Government Medical College, Amritsar from October 2015 to January 2017. Children were divided into 2 groups of A and B randomly and were given nebulisation with 3% saline and L-adrenaline respectively at 0, 30 mins and 1 hour followed by 6hrly a day till hospital stay. Bronchiolitis clinical severity scoring was done on admission, 0, 30 mins,1 hour and thereafter once daily till discharge along with monitoring of vitals and clinical condition.

The efficacy of the two treatments were compared in terms of the following parameters:

1. Reduction in respiratory scores compared to baseline in each of the groups. Scores were compared at two therapeutic points , one done at 1 hour of presentation i.e after 3 nebulisations and the other at discharge.
2. Duration of hospital stay in both groups.

**Results:** The average baseline Clinical Severity scores in 3% saline and adrenaline groups were 6.3+- 1.9 and 5.9+- 2.7 respectively. Scores at 1hr and discharge respectively were 3.9+-1.4 , 1.4+-0.9 in 3% saline group and 4.4+-1.9 , 2.3+-1.4 in adrenaline group. On statistical analysis the fall in clinical scores compared to baseline was significantly more in 3% group both at 1 hr and discharge.

**Conclusion:** We found nebulised 3% saline as superior to nebulised adrenaline in efficacy in acute bronchiolitis, the difference in clinical severity scores being significant at 1hour of presentation and discharge. The time to complete clinical recovery was less in case of 3% saline with early hospital discharge.

**Keywords:** Hypertonic saline, L- adrenaline, 3% saline vs nebulised L- adrenaline, acute bronchiolitis.

## Introduction

Acute bronchiolitis is a common lower respiratory tract disease affecting children under 2 years of age[1]. The most commonly involved age group is 3-6 months[2]. Most cases of bronchiolitis result from a viral pathogen, such as respiratory syncytial virus(RSV), rhinovirus, human metapneumovirus (hMPV), parainfluenza virus, adenovirus, coronavirus, influenza virus or human bocavirus[2]. In one third of hospitalized cases of bronchiolitis, two or more viruses may be detected, especially when using molecular-based testing. RSV is the most commonly isolated agent in 75% of children younger than 2 years who are hospitalized for bronchiolitis[2]. RSV is an enveloped RNA virus that belongs to the Paramyxoviridae family within the Pneumovirus genus. RSV causes 20-40% of all cases and 44% of cases that involve children younger than 2 years. Bronchiolar injury and the consequent interplay between inflammatory and mesenchymal cells can lead to diverse pathologic and clinical syndromes. The effects of bronchiolar injury may begin 18 to 24 hours after the infection and include the following[7]:

- Increased mucus secretion
- Bronchial obstruction and constriction
- Alveolar cell death, mucus debris, viral invasion
- Air trapping
- Atelectasis
- Reduced ventilation that leads to ventilation-perfusion mismatch

Acute bronchiolitis usually occurs after exposure to a patient with minor respiratory symptoms. Infant first develops a mild upper respiratory infection with nasal discharge and cough. This is followed by decreased feeding followed by respiratory distress. Apnea can be a feature in young infants[8]. Diagnosis is a clinical one[9] with features of nasal flaring , tachypnea , retractions with auscultatory finding of wheezing or prolonged expiration with crepts[7]. Chest radiographs can show hyperexpansion or atelectasis due to air trapping.

Since the outset, treatment of bronchiolitis consisted of humidified oxygen, with i.v fluids and nutrition. Bronchiolitis is a self limiting disease[10] and most often no treatment modality seems to work definitively. Despite the availability of practice guidelines for bronchiolitis, there is still variation and controversy among healthcare providers regarding the optimal treatment of these patients.

There have been insufficient evidence regarding the use of antibiotics, bronchodilators, recombinant DNAase[11], corticosteroids, ribavirin[12] or surfactant[13] in acute management of bronchiolitis. Recent studies have suggested hypertonic saline as an emerging modality showing promising results in bronchiolitis.

L-adrenaline is also a potential treatment option in acute bronchiolitis. Wohl and Chernick postulated that, since mucosal edema was an important component of airway obstruction in infants with bronchiolitis, a logical approach to therapy might be to use a combined α-adrenergic and β-adrenergic agonist, such as epinephrine[14].Many studies have been conducted regarding efficacy of adrenaline[15] as well as its comparison to other modalities like bronchodilators and nebulised

steroids. Being a relatively inexpensive and readily available option we felt need to gather more evidence in this regard by comparing the efficacy of adrenaline with hypertonic saline.

## Materials and Methods

This prospective study was conducted on 100 children admitted with acute bronchiolitis in the department of Pediatrics, Government Medical College, Amritsar from December 2015 to January 2017. Randomisation was done using research randomizer software and a unique set of numbers were generated for both interventional groups L-adrenaline and 3%hypertonic saline.

### Inclusion criteria

1. Age group 1 month to 2 yrs.
2. First episode of wheezing.
3. History of viral prodrome present.
4. Bronchiolitis disease severity score>4.
5. No history of treatment with either nebulised 3% saline or L-adrenaline during the disease course.

### Exclusion criteria

1. Wheezing children < 1month or > 2yrs.
2. Evidence of bacterial infection or clinical course not compatible with acute bronchiolitis.
3. Family history of asthma.
4. Congenital heart disease or chronic lung disease.

Children were divided into 2 groups of A and B as per randomization technique and were given nebulisation with 3% saline and L-adrenaline respectively at 0, 30 mins and 1 hour followed by 6hrly a day till hospital stay. Dose of adrenaline used was 0.5 ml of 1:1000 solution in 3.5ml of normal saline.3% saline was given in a volume of 4ml per nebulisation. Bronchiolitis respiratory scoring was done on admission, 30 mins,1 hour and thereafter once daily till hospital stay along with monitoring of vitals and clinical condition.

TABLE 1: Bronchiolitis clinical severity score[16].

| | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| Respiratory Rate | <30 | 31-45 | 46-60 | >60 |
| $SaO_2$ | ≥ 90 % | ≥ 88 % | ≥ 86 % | ≤ 85 % |
| General Appearance | Calm No distress | Mildly irritable; easy to console | Moderately irritable; difficult to console | Extremely irritable; cannot be comforted |
| Retractions and nasal flaring (NF, SS, IC, SC) | None | 1 of 4 | 2 of 4 | 3 or more |
| Auscultation | Clear | Scattered wheezes | Diffuse expiratory wheezing | Biphasic wheezing or very poor air movement |

## Results

### 1. Patient parameters:

**Age distribution:** Out of 50 random patients chosen for each group of treatment, the age distributions were:

**Table 1**

| | 1-6 months | 6-12 months | 12months-2years |
|---|---|---|---|
| 3% saline group | 34 | 13 | 3 |
| Adrenaline group | 40 | 8 | 2 |

**Gender distribution:**

**Table 2**

| | Males | Females |
|---|---|---|
| 3% saline group | 36 | 14 |
| Adrenaline group | 32 | 18 |

**Baseline clinical severity scores**:

**Table 3**

| | Baseline CS score |
|---|---|
| 3% saline group | 6.2+- 1.8 |
| Adrenaline group | 5.4+-2.6 |

**Duration of illness prior to admission:**

**Table 4**

| | Duration of illness prior to admission |
|---|---|
| 3% saline group | 2.5+-1.4 |
| Adrenaline group | 3.3+-1.6 |

### 2. Treatment parameters:

**Change in clinical severity scores:** **Table 5**

| CS score | 1hour | Discharge |
|---|---|---|
| 3% saline group | 3.8+-1.3, p<0.01 | 1.3+-1.4, p<0.01 |
| Adrenaline group | 4.3+-1.8 | 2.2+-1.4 |

**Duration of hospital stay:**

**Table 6**

| Hospital stay | Days |
|---|---|
| 3% saline group | 3.7+-2.0 |
| Adrenaline group | 4.0+-2.2 |

**p=0.05**

## Discussion

Statistically p value<0.05 was considered significant. The following analysis was made:

**Age:** In our study out of 50 patients included in either treatment groups, majority were of age group 1-6 months. This number was 68% and 80% respectively in hypertonic saline and adrenaline groups respectively. This was consistent with other studies like Kuzik et al[17], Mandelberg et al[18] and Guy Tal et al[19] in which also majority infants were from the same age group. Other studies like Grewal et al and Sarell et al[20] found mean age to be 6-12 months. The infants with RSV infection in this age group have greater propensity to wheeze because of small caliber of airways. The resistance to airflow is more as it varies as 4$^{th}$ power of radius of airway. Since our diagnosis in this study was based on auscultatory finding of wheezing, this was consistent with majority of infants being included in age group 1-6 months. The number decreased progressively in age group 6-12 months and 1-2 years as airways grow in size and propensity to wheeze decreases.

### Gender:

The patients included in 3% saline group were 72% males and in adrenaline group were 64% males. This is in accordance with the known fact that bronchiolitis affects more males as compared to females. Previous studies by Kuzik et al[17] and Som et al[21] also had similar findings.

The greater incidence in males as compared to females may be attributed to presence of 2 X chromosomes which produce greater genetic diversity to the female immunologic defences.

### Duration of illness prior to hospital admission:

The duration of illness prior to admission was 2.5+-1.4 in 3% saline group and 3.3+-1.6 in adrenaline group . In previous studies by Guy Tal et al[19] and Manderberg et al[18] this duration was found to be 4.5+-2 days and 3.0+-1.6 days respectively. As patients under study were from the same environment and factors affecting individual to counteract the disease were identical, the 2 groups were comparable.

### Baseline clinical severity scores:

The baseline clinical severity scores in 3% saline and adrenaline group were 6.2+-1.8 and 5.4+-2.6 respectively. The p value was 0.105. Hence both groups before intervention were comparable.

### Change in clinical severity scores:

In our study we found that decrease in clinical severity scores in 3% saline was significantly more compared to adrenaline. The scores at 1hr of nebulisation as well as on discharge were better in saline group (p=0.001). Many previous studies have been conducted on the efficacy of adrenaline alone in bronchiolitis. The findings have yielded variable results. Study by S Kristjansson and KC Lodrup[22] have shown it to be better compared to placebo. Other studies like Abil ,Luyt[23] ,april 2002; Hariprakash S[24] April 2003 have found no efficacy compared to saline or placebo. Except these studies some comparative trials of adrenaline have also been conducted. In 2009 nov, RCT of nebulised 3% saline + adrenaline vs adrenaline in normal saline was done and concluded similar efficacy of both modalities. Another randomized controlled trial by Kusum Menon and Teresa Sutcliffe[25] compared adrenaline with salbutamol and found adrenaline to be superior. Other studies like BM John[26], October 2006 had similar results finding adrenaline to be superior to salbutamol.

We found very few comparative studies of hypertonic saline and adrenaline together. One similar study was conducted by J Carlos Forbes and Miguel A[27] comparing 3% saline with adrenaline+3% saline and found that adrenaline added to the efficacy and the combination was superior compared to hypertonic saline alone.

Besides having a common mechanism of action of decreasing airway edema, hypertonic saline and adrenaline differ in other functions. 3% saline is known to improve mucus clearance, increase coughing action, making the mucus less viscous, increasing ciliary action as well as decreasing

bacterial colonization[28]. Adrenaline on the other hand acts by vasoconstriction and decreasing airway edema and inflammation. It is perhaps due to these additional mechanisms of action that hypertonic saline showed more efficacy in our study during treatment. Therefore whereas adrenaline might have a synergistic role when given along with 3% saline, alone its efficacy is less than hypertonic saline. However since adrenaline acts to reduce mucosal edema and inflammation it may be superior to placebo or bronchodilators in managing bronchiolitis. Besides , 3% saline has no systemic affects and acts locally, therefore ensured a better safety profile compared to adrenaline.

### Duration of hospital stay:

Hypertonic saline also reduced the duration of hospital stay as compared to adrenaline. The mean duration of stay was 3.7+-2.0 and 4.0+-2.2 respectively. However the difference was not found to be statistically significant. Perhaps hospital stay was influenced by other factors like transition to oral feeding, gaining proper appetites and ensuring weight gain before discharge. Associated factors like fedding habits, use of top feeds, anemia etc also played a role in these infants to prolong the hospital stay.

## Conclusion

It is concluded from our study that nebulised hypertonic 3% saline is a better treatment modality in comparison to nebulised adrenaline in acute bronchiolitis. Infants treated with 3% saline showed greater improvement and early hospital discharge. This may be due to additional mechanisms by which hypertonic saline acts in bronchiolitis like increasing ciliary beat frequency, release of prostaglandins[28] etc. Hence as per our study hypertonic 3% saline may be used as a preferable treatment option along with conventional humidified oxygen and i.v fluids. Lack of systemic side effects, ease of administration and a good safety profile with easy availability makes it a promising option compared to adrenaline in cases of acute bronchiolitis. However further studies can be done assessing efficacy of combined adrenaline and hypertonic saline. Since these have similar mechanisms of action there is a possibility of a potential synergistic role with 3% saline.

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## References

1. Klassen TP. Recent advances in the treatment of bronchiolitis and laryngitis.Pediatr Clin North Am.1997;44:249-61
2. Kabra SK, Ghai OP. Respiratory disorders.In: Ghai OP ,Gupta P, Paul VK,Ghai Essential pediatrics. 8th edn. New Delhi: CBS Publishers & Distributors, 2013,p.376-8.
3. Mathew JL. Hypertonic saline nebulisation for bronchiolitis. Indian Pediatr.2008;45(12): 987-9
4. Zhang L,Mendoza Sassi RA,Wainwright C.Nebulised hypertonic saline solution for acute bronchiolitis in infants.Cochrane Database Syst Rev.2008;(4) CD006458.
5. Menon K,Sutcliffe T,Klassen TP. A randomized trial comparing efficacy of epinephrine with salbutamol in the treatment of acute bronchiolitis. J Pediatr. 1995;126:1004-7.
6. Handforth J, Friedland JS, Sharland M. Basic epidemiology and immunopathology of RSV in Children.Pediatric Respiratory Reviews. 2000;1:210-14.
7. Kimberly DW,Goodman DM. Wheezing, Bronchiolitis and Bronchitis In : Kleigman RM,Behrman RE,Jeon HB,Stanton BF eds.Nelson Textbook of Pediatrics.19th edn.New Delhi : Elsevier,2011,p.1456.
8. Kliegman RM, Stanton BF, St. Geme JW, Schor NF, Behrman RE. Status epilepticus. In: Nelson Textbook of Pediatrics,20th Ed.Elsevier; 2015.p.2047.
9. Ralston SL,Lieberthal AS,et al.Clinical Practice Guideline: The Diagnosis,Management and Prevention of Bronchiolitis.Pediatrics.2014 Oct27.[Medline].
10. Dennis MM. Bronchiolitis.Arch Dis Child Educ Pract.2005;90:81-6.
11. Nasar SZ, Strouse PJ, Soskoline E,Maxvold NJ, Graver KA.Efficacy of recombinant human deoxyribonuclease in the hospital management of RSV bronchiolitis.Chest.2001;120:203-8.
12. Ventre K, Randolphh AG.Ribavirin for respiratory syncytial virus infection of the lower respiratory tract in infants and young children. Cochrane database of Sys Rev.2004;4:4.

13.Jat KR,Chawla D.Surfactant therapy for bronchiolitis in critically ill patients.Cochrane Database Syst Rev.2015 Aug24.8:CD009194.
14.Woht ME, Chernick V. State of the art: bronchiolitis. Am Rev Respir Dis 1978;118:759-81.
15.Numa AH,Williams GD, Dakin CJ. The effect of nebulized epinephrine on respiratory mechanics and gas exchange in bronchiolitis.Am J Respir Crit Care Med.2001;164:86-91.
16.Wang EEL,Milner RA,Navas L, Maj H.Observer agreement for respiratory signs and oximetry in infants hospitalized with lower respiratory infections. Am Rev Respir Dis.1992;145:106-9.
17.Kuzik BA ,Al Qadhi SA,Kent S, Flavin MP, Hopman W, Hotte SA.Nebulized hypertonic saline in the treatment of viral bronchiolitis in infants. J Pediatr. 2007; 151(3):266-70.
18.Mandelberg A,Tal G Witzling M, Somexk E, Houri S, Balin A. Nebulized 3% hypertonic saline solution treatment in hospitalized infants with viral bronchiolitis. Chest. 2003;123:481-7.
19.Tal G, Cesar K, Oron A, Houri S, Ballin A, Mandelberg A. Hypertonic saline/ epinephrine treatment in hospitalized infants with viral bronchiolitis reduces hospitalization stay: 2 years experience. IMAJ. 2006;8: 169-73.
20.Sarrell EM, Tal G, Witzling M, Someck E, Houri S, Cohen HA. Nebulized 3% hypertonic saline solution treatment in ambulatory children with viral bronchiolitis decreases symptoms. Chest. 2002;122:2015-20.
21. Ray MS and Singh V. Comparison of nebulized adrenaline versus salbutamol in wheeze associated respiratory tract infection in infants. Indian Pediatr. 2002; 39: 12-22.
22. Kristjansson S,Lodrup KC: Nebulised racemic adrenaline in the treatment of acute bronchiolitis in infants and toddlers. Archives of disease in childhood 1993;69:650-54.
23. Abil A, Luyt D. Short term effects of adrenaline in bronchiolitis: A randomized controlled trial 2002, April;86(4):276-79.
24.Hariprakash S, Alexade J.A randomized controlled trial of nebulised adrenaline in acute bronchiolitis.2003. April;14(2): 134-9.
25. Kusum M, Sutcliffe T. A randomized trial comparing the efficacy of epinephrine with salbutamol in the treatment of acute bronchiolitis. The Journal of Pediatrics, June1995; vol 126(6):1004-7.
26. John BM, Patnaik SC. Efficacy of Nebulised Epinephrine versus Salbutamol in Hospitalised Children with Bronchiolitis. Medical Journal Armed Forces India , Oct2006;vol62(4):354-57.
27.Carlos J, Miguel A. Epinephrine Improves the Efficacy of Nebulized Hypertonic Saline in Moderate Bronchiolitis: A Randomised Clinical Trial. Plos One.2015;10(11):0142847. doi: 10.1371/journal.pone.0142847.
28. Mandelberg A, Amrav I.Hypertonic Saline or High Volume Normal Saline For Viral bronchiolitis. Pediatric Pulmon.2010;45:36-40.

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