

A Comparative Study on Use of 3% Saline Versus 0.9% Saline Nebulization in Children with Bronchiolitis

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ABSTRACT

Background: Bronchiolitis is a common clinical problem in children below 2 years presenting with respiratory symptoms. As there is necrosis and sloughing of epithelial cells, edema, increased secretion of mucus causing obstruction of large and small airways we aim to see the clinical profile and the effect of use of hypertonic (3%) saline nebulization in these children.

Methods: A double blind randomized controlled trial was conducted at department of Pediatrics, in a hospital from July 2012 to August 2013. The computer generated random number was used to select the case and control group. All eligible patients were randomly assigned to one of two groups: receiving inhalation of 4 ml normal (0.9%) saline or hypertonic (3%) saline. Treating physicians, researchers and nurses were all blinded of the solution. Both saline were kept in two identical containers and labeled as solution A and solution B. Patients in each group will receive three treatments on each day of hospitalization and clinical score were obtained 30 minutes before each inhalation session.

Results: Bronchiolitis accounted 11.26% of total admissions. Their mean age (\pm SD) was 8.56 (\pm 5.013) months with range from 45 days to 24 months. A total of 53 (74%) male were enrolled in the study. Fifty-seven (79%) children were less than 12 months and 15 (21%) were 12 months - 24 months. The mean (\pm SD) for duration of hospital stay was 44.82 (\pm 23.15) and 43.60 (\pm 28.25) for 3% and 0.9% group respectively ($p=0.86$). Likewise, mean (SD) duration of oxygen supplementation was 32.50 (\pm 20.44) and 34.50 (\pm 26.03) for 3% and 0.9% group respectively ($p=0.85$). Moreover, time required for normalization of clinical score was 36.79 (\pm 19.53) and 38.34 (\pm 26.67) for 3% and 0.9% group respectively ($p=0.80$).

Conclusions: There is no advantage of hypertonic saline over normal saline nebulization in the management bronchiolitis.

Keywords: bronchiolitis; hypertonic saline; nebulization.

INTRODUCTION

Bronchiolitis is a common clinical problem in children below 2 years presenting with tachypnea, and increased work of breathing, follow the upper respiratory prodrome and physical findings of nasal congestion, rhinorrhea, cough, tachypnea, and increased respiratory effort characterized by nasal flaring, grunting, and intercostal, supracostal, and subcostal retractions.¹ It is characterized by inflammation of the bronchioles following an acute viral infection.²

In bronchiolitis there is necrosis and sloughing of epithelial cells, edema, increased secretion of mucus, and peribronchiolar mononuclear infiltration - changes that obstruct flow in the large and small airways, leading to hyperinflation, atelectasis and wheezing.^{1,3} There are studies to ameliorate this pathophysiology with inclusion of bronchodilators⁴⁻⁹ and also steroids^{10,11} in the treatment. Unfortunately those inclusions did not have positive impact. Studies have shown that hypertonic

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saline improves mucus rheologic properties (elasticity and viscosity) and accelerates mucus transport rates.¹² Its inhalation increases the volume of airway surface liquid and increases rates of mucociliary clearance in normal subjects.¹³ A study conducted in infants with viral bronchiolitis demonstrated the effectiveness of hypertonic saline as a treatment agent.¹⁴ However there are very few studies on this subject. This double blind controlled study was undertaken to see the role of nebulized hypertonic saline in bronchiolitis and also the clinical profile in these children.

METHODS

A double blind randomized controlled trial was conducted at department of Pediatrics, Kathmandu Medical College, Sinamangal, Kathmandu for a duration of 13 months (July 2012 to August 2013). The objective of the study was to determine whether nebulized 3% hypertonic saline is more effective than nebulized 0.9% saline in the treatment of bronchiolitis. We compared the length of hospital stay, duration of oxygen supplementation and duration required for normalization of a respiratory distress score between 3% and 0.9% normal saline nebulized groups. We also intended to look at the clinical profile in these children. The sample size for this study was 72:36 in case and control group. This was calculated using PS-Power and Sample Size Calculator Version 3.0.43.

Children older than 6 weeks and below 24 months with clinical presentation of bronchiolitis for the first time were included in the study. Those who had previous episode of wheezing, chronic cardiac and pulmonary disease, immunodeficiency, accompanying respiratory failure, requiring mechanical ventilation, inhaling the nebulized 3% hypertonic saline solution and salbutamol 12 hr before treatment, premature infants born at less than 34 weeks gestation, children who have oxygen saturation below 85% on room air and were excluded. The study was conducted after obtaining ethical clearance from Nepal Health Research Council.

All the data were entered in excel and transferred to SPSS version 17. In descriptive statistics, the data were presented by percentage, mean and standard deviation. T-test was used to compare the means from the two groups i.e. 3% and 0.9% saline. Chi-square test was used to compare proportion difference between two groups. A P-value < 0.05 considered statistically significant.

All the children diagnosed as bronchiolitis and who fulfill the inclusion criteria were included after informed consent from the parent(s). The case was defined as bronchiolitis if it was the first episode of wheezing associated with tachypnea, increased respiratory effort and an upper respiratory tract infection.¹⁵

All children were thoroughly examined. Children were admitted who have the clinical scoring of respiratory distress of ≥ 4 .¹⁶ The following parameters were measured and recorded using the clinical score: respiratory rate, wheezing, retraction, and oxygen saturation. This scoring system assigns a number from 0 to 3 to each variable with increased severity receiving a higher score. All patients were enrolled within 24 hours of admission to the hospital.

Table 1. Clinical scoring used in this study.¹⁶

Score	Respiratory rate (breaths/minute)	Wheezing	Accessory respiratory muscle retraction	Oxygen saturation
0	≤ 30	None	None	$\geq 95\%$
1	31-45	Terminal expiration with stethoscope only	Flaring of ala nasii	90-94%
2	46-60	Entire expiration and inspiration with stethoscope only	Suprasternal	85-89%
3	> 60	Expiration and inspiration without Stethoscope	Suprasternal plus intercostal plus subcostal	$< 85\%$

The patients were selected by a double-blind randomization. The computer generated random number was used to select the case and control group. The random numbers were kept in a sealed envelope. The attending nurse or physician drew the envelope and get the treatment (hypertonic saline or normal saline) accordingly. Thus all eligible patients were randomly assigned to one of two groups: Group I received inhalation of 4 ml normal (0.9%) saline and group II got inhalation of 4 ml hypertonic (3%) saline. 3% saline and 0.9% saline were kept in two identical containers. The two solutions were labeled as solution A and solution B. This labeling was done by a sister who was not involved in care to patients in the ward. The solutions looked similar in appearance and smell, labeled only by a code number, and placed in the research cupboard. The randomization list was concealed until completion of the study. So the emergency physicians, house staff, nurses, study personnel, and patients were blinded to treatment allocation throughout the study.

Patients in each group received minimum of three nebulization each day delivered at eight hours interval, until discharge. Additional nebulization or other additional treatment for these children was left to the decision of the treating Pediatrician. However the treating doctor was blinded of the two groups. Any child with oxygen saturation below 92% at room air received supplemental oxygen. At treatment time and 30 minutes before the beginning of each inhalation session, clinical score was obtained.

Patients were discharged when there was no requirement of supplementary oxygen, feeding adequately without intravenous fluids, and had minimal or absent wheezing, crackles, and chest retractions, provided that oxygen saturation was $\geq 95\%$ at room air for 4 hours and the severity score was < 4 .¹⁶

The length of hospital stay was calculated from the time of entry of the case in the study to time of discharge. Similarly the duration of oxygen supplementation and the time period required to fall the clinical score below 4 was recorded in both the groups.

RESULTS

In total, 1172 children were admitted in the Pediatric ward with various diagnoses during the study period. Out of these 104 (11.26%) children were diagnosed with bronchiolitis.

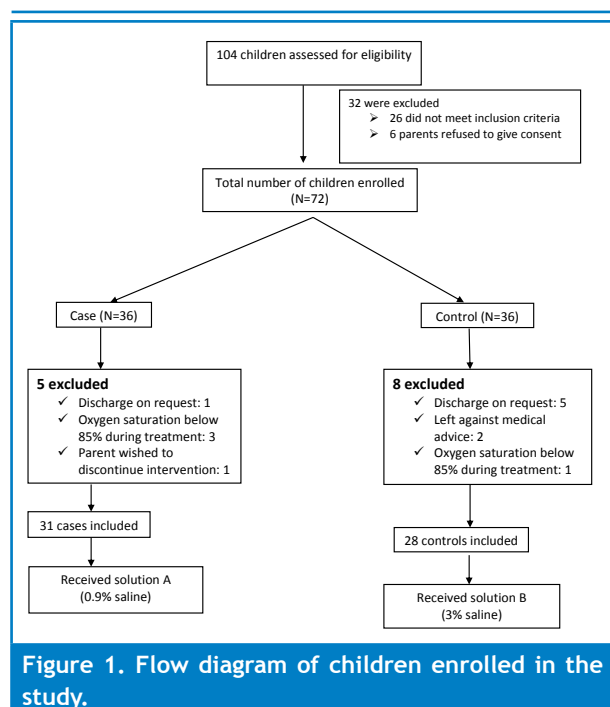


Figure 1. Flow diagram of children enrolled in the study.

The baseline characteristics of the two groups who received 3% saline or 0.9% saline were comparable (Table 2).

Table 2. Baseline characteristics of study population.

Variables	3% saline	0.9% saline	p-value
Male/Female (number)	36	36	0.789
Age (mean)(\pm SD)	8.61 (\pm 5.742)	8.51(\pm 4.24)	0.935
Antibiotic usage(number)	22	23	0.808
Steroid use(number)	5	6	0.743
Baseline score (mean) (\pm SD)	8.08 (\pm 1.68)	7.36 (\pm 1.91)	0.093
Baseline oxygen saturation (mean) (\pm SD)	91.47 (\pm 1.68)	90.58 (\pm 1.91)	0.547
Baseline respiratory rate (mean)(\pm SD)	59.28 (\pm 10.48)	59.81 (\pm 9.94)	0.827
Additional nebulization (mean)(\pm SD)	1.89 (\pm 1.81)	1.77 (\pm 2.30)	0.828

There is a fall in clinical score between two groups after commencement of the treatment. However the fall is not statistically significant (Figure 2).

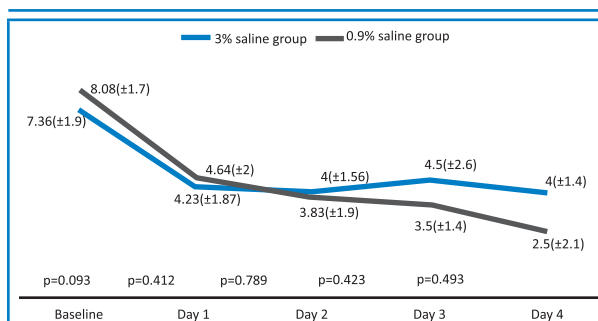


Figure 2. Graphical presentation of mean (\pm SD) clinical respiratory score on different days of intervention between two groups of children.

There are 31 and 28 patients in 0.9% saline and 3% saline group respectively who completed the treatment. The average (\pm SD) duration of hospital stay in these two groups were 43.60(\pm 28.25) hours and 44.82(\pm 23.15) hours respectively which is not statistically significant ($p=0.86$).

Out of 72 children, 21 required oxygen supplementation. Twelve of 21 children received 3% saline and remaining nine obtained 0.9% saline nebulization. The mean (\pm SD) duration of oxygen supplementation was 32.50(\pm 20.44) hours and 34.50(\pm 26.03) hours in 3% and 0.9% groups respectively, which is not statistically significant ($p=0.85$).

Children who received 3% saline and 0.9% saline took 36.79 (± 19.53) hours and 38.34 (± 26.67) hours respectively to have their clinical score to fall below score of 4. This is again statistically not significant ($p=0.80$).

Majority of the cases of bronchiolitis occurred during the months of November to February. The following chart shows the month wise frequency of cases throughout the year (Figure 3).

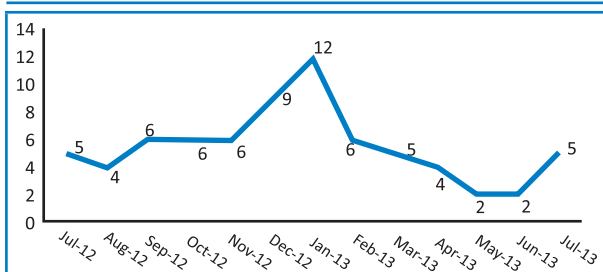


Figure 3. Month wise distribution of cases.

DISCUSSION

Bronchiolitis is a common lower respiratory tract infection in infants and is most frequently caused by the RSV. In our study, bronchiolitis accounted 11.26% of total hospital admissions. The mean age of children involved in our study was 8.563 (± 5.0126) months with range from 45 days to 24 months 79% of children were below 12 months. In a study by Mecklin M et al the mean age of children was 12.7 months.¹⁷ 74% of the children involved in our study were male. This is comparable to study done by Kuzik BA et al¹⁸ which accounted for 62%.

The bulk of the cases in our study were admitted during the month of December. Zlateva KT et al in their study also found the peak incidence of bronchiolitis during December¹⁹ which corroborates to our finding.

There was no significant statistical difference in demographic characteristics of the groups of children who received 3% saline or normal saline. Also there was no difference in two groups on baseline respiratory distress score, baseline respiratory score, and baseline oxygen saturation.

Children involved in our study were scheduled to receive nebulization three times in a day. However the treating physician could add more nebulization if needed. Also it was in the decision of the treating Pediatrician to add on any other treatment. In this regard, in 3% saline group, 22 children received antibiotics, 5 received steroid (inhalational or oral) and 28 received additional nebulization. Similarly, in 0.9% saline group, 23 received antibiotics, 6 received steroid (inhalational or oral) and 31 received additional nebulization. These extra

additions did not have any impact on the intervention outcome, as they were all statistically not significant.

In our study group, nebulization with 3% hypertonic saline did not prove superiority to 0.9% saline for improving the bronchiolitis severity score in patients with viral bronchiolitis ($p=0.801$). Moreover it did not have any significant impact on reduction of hospital stay ($p=0.859$) and reduction of oxygen supplementation duration ($p=0.846$). Unlike our study, a Cochrane review states that nebulized hypertonic saline with bronchodilators was considered an effective and safe treatment for infants with viral bronchiolitis.²⁰ A study done by Mandelberg A et al in 2003, use of hypertonic saline reduces clinical symptoms, shortens the length of hospitalization, and reduces the clinical severity score.¹⁵ Moreover there are other studies, which showed a better outcome in children who were nebulized with hypertonic saline.^{21, 22} However, study by Sharma BS et al in their study showed no advantage of hypertonic saline in clinical severity scores and mean length of hospital stay over normal saline nebulization.²² Ipek IO et al in their study also found the similar results.²⁴ These findings corroborate our finding.

In our study we observed that the clinical score fell very sharply in the first 48 hours of nebulization, in both the groups, even though it was statistically not significant. However the trend of fall of the distress score was not sharp after 48 hours of inhalation. Study by Sarnell EA et al in their study also revealed the same finding.²¹ We did not notice any side effects in children treated with either solution.

There are few limitations of our study. There was difficulty in asserting the diagnosis of bronchiolitis, as we did not have any diagnostic tool to identify the virus. Our diagnosis was purely clinical. Though we enrolled only those children who had first episode of wheezing, at times it can be misleading that there is a good chance that the child could be a first episode of asthma.

CONCLUSIONS

Bronchiolitis is a common cause of Pediatric admission during infancy. There is no advantage of hypertonic saline over normal saline nebulization in the management as it did not reduced the duration of hospital stay, did not help in better reduction of respiratory distress score and did not decreased the oxygen requirement duration. However, this finding needs further validation using large sample size.

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REFERENCES

1. American Academy of Pediatrics, Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics*. 2006;118(4):1774–93.
2. Wagner T. Bronchiolitis. *Pediatr. Rev.* 2009;30:386–95.
3. Hall CB. Respiratory syncytial virus and parainfluenza virus. *N Engl J Med.* 2001;344:1917–28.
4. Klassen TP, Rowe PC, Sutcliffe T, Ropp LJ, McDowell IW, Li MM. Randomized trial of salbutamol in acute bronchiolitis. *J Pediatr.* 1991;118:807–11.
5. Schuh S, Canny G, Reisman JJ, Kerem E, Bentur L, Petric M, et al. Nebulized albuterol in acute bronchiolitis. *J Pediatr.* 1990;117:633–7.
6. Schweich PJ, Hurt TL, Walkley EI, Mullen N, Archibald LF. The use of nebulized albuterol in wheezing infants. *Pediatr Emerg Care.* 1992;8:184–8.
7. Alario AJ, Lewander WJ, Dennehy P, Seifer R, Mansell AL. The efficacy of nebulized metaproterenol in wheezing infants and young children. *Am J Dis Child.* 1992;146:412–8.
8. Gadomski AM, Lichenstein R, Horton L, King J, Keane V, Permutt T. Efficacy of albuterol in the management of bronchiolitis. *Pediatrics.* 1994;93:907–12.
9. Wang EEL, Milner R, Allen U, Maj H. Bronchodilators for treatment of mild bronchiolitis: a factorial randomized trial. *Arch Dis Child.* 1992;67:289–93.
10. Klassen TP, Sutcliffe T, Watters LK, Wells GA, Allen UD, Li MM. Dexamethasone in salbutamol treated in-patients with acute bronchiolitis. *J Pediatr.* 1997 Feb;130(2):191–6.
11. Plint AC, Johnson DW, Patel H, Wiebe N, Correll R, Brant R, et al. Pediatric Emergency Research Canada (PERC). Epinephrine and dexamethasone in children with bronchiolitis. *N Eng J Med.* 2009 May 14;360(20):2079–89.
12. Darville T, Yamauchi T. Respiratory syncytial virus. *Pediatr Rev.* 1998;19:55–61.
13. Wills PJ, Hall RL, Chan W, Cole PJ. Sodium chloride increases the ciliary transportability of cystic fibrosis and bronchiectasis sputum on the mucus-depleted bovine trachea. *J Clin Invest.* 1997;99:9–13.
14. Sood N, Bennett WD, Zeman K. Increasing concentration of inhaled saline with or without amiloride: effect on mucociliary clearance in normal subjects. *Am J Respir Crit Care Med.* 2003;167:158–63.
15. Mandelberg A, Tal G, Witzling M. Nebulized 3% hypertonic saline treatment in hospitalized infants with viral bronchiolitis. *Chest.* 2003;123:481–7.
16. Teeratakulpisam J, Limwattananon C, Tanupattarachai S, Limwattananon S, Teeratakulpisam S, Kosalaraksa P. Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: a randomized, double-blind, placebo-controlled trial. *Pediatr Pulmonol.* 2007 May;42(5):433–9.
17. Mecklin M, Hesselmar B, Wennergren G, Korppi M. Diagnosis and treatment of bronchiolitis in Finnish and Swedish children's hospitals. *Acta Paediatr* 2014 Apr 29. doi: 10.1111/apa.12671. [Epub ahead of print]
18. Kuzik BA, Al-Qadhi SA, Kent S. Nebulized hypertonic saline in the treatment of viral bronchiolitis in infants. *J Pediatr.* 2007;151:266–70.
19. Zlateva KT, Vijgen L, Dekeersmaecker N, Naranjo C, Van Ranst M. Subgroup prevalence and genotype circulation patterns of human respiratory syncytial virus in Belgium during ten successive epidemic seasons. *J Clin Microbiol.* 2007 Sep;45(9):3022–30.
20. Zhang LJ, Mendoza-Sassi RA, Wainwright C. Nebulized hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database Syst. Rev.* 2008;8:CD006458.
21. Sarnell EM, Tal G, Witzling M, Someck E, Houry S, Cohen HA, Mandelberg A. Nebulised 3% hypertonic saline solution treatment in ambulatory children with viral bronchiolitic decreases symptoms. *Chest.* 2002;122:2015–20.
22. Zhengxiu Luo, Enmei Liu, Jian Luo, Subi Li, Fengqiong Zeng, Xiqiang Yang, et al. Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. *Pediatrics International.* 2010;52:199–202.
23. Sharma BS, Gupta BK, Rafik SP. Hypertonic(3%) saline Vs 0.9% saline nebulization for acute viral bronchiolitis: A randomized controlled trial. *Indian Pediatrics.* 2013 Aug;50:743–7.
24. Ipek IO, Yalcin EU, Sezer RG, Bozaykut A. The efficacy of nebulized salbutamol, hypertonic saline and salbutamol/hypertonic saline combination in moderate bronchiolitis. *Pulm Pharmacol Ther.* 2011 Dec;24(6):633–7.