

Comparison of Mean Hospital Stay after Nebulization with 3% Hypertonic Saline vs Salbutamol in Treatment of Bronchiolitis

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Abstract: Background: With an estimated prevalence of 33% in children age >2years and owing to 1 in 10th cause of hospitalization in children, Bronchiolitis is a major factor for morbidity and mortality. Varying nebulization doses have been shown to produce different clinical outcomes in patients with bronchiolitis.

Objective: To compare mean hospital stay after nebulization with 3% hypertonic saline compared to the salbutamol among patients of bronchiolitis

Materials and Methods: This was a randomized control study done at pediatric medicine ward, Services Hospital, Lahore. The study was done during 8th May 2018 to 8th November 2018. Data was collected from 68 children of age >3 months to < 2 years of both genders i.e. (34 in each group) fulfilling inclusion criteria. SPSS software was used for data entry and analysis. For quantitative variables age, mean and standard deviation were used whereas for qualitative variables like gender, frequency and percentages were used. Independent sample t-test was used for comparing mean hospital stay among the two groups taking p-value<0.05 as significant.

Result: Average age in Salbutamol group was 1.06 ± 0.50 years and in Hypertonic solution mean age was 1.24 ± 0.55 years. There was significant difference in mean hospital stay with relatively lesser in hypertonic solution vs the Salbutamol group [3.18 ± 1.11 vs 4.44 ± 1.08 ; p-value <0.001]. Upon post-stratification analysis, the mean hospital stay was found to be significantly lower in the Hypertonic group vs. Salbutamol group with respect to age, gender and the duration of the disease (p-values<0.05 for all).

Conclusion: This study concludes that the mean hospital stay was statistically lower in the hypertonic solution group vs the Salbutamol group. Moreover, the clinical efficacy of the hypertonic saline can be utilized in future to gain early recovery of Bronchiolitis and hence it can reduce the hospital stay and related cost.

Keywords: Bronchiolitis, Salbutamol, Hypertonic saline, Hospital stay, Severity, Duration, Treatment.

INTRODUCTION

According to WHO, the Bronchiolitis is defined as respiratory infection characterized by wheezing and struggle of breathing among the children under 2 years of age [1]. Approximately 33% of the children <2 years of age suffer from bronchiolitis. It is estimated that every 1 of 10 children need hospitalization due to bronchiolitis [2]. In the United States alone, more than 100,000 hospital stay is reported every year for children under 2 years due to bronchiolitis with \$1.73 billion estimated hospital cost [3, 4]. Moreover, Bronchiolitis is responsible for considerable morbidity as well as mortality due to a number of complications [5]. If not treated timely, the chance of these respiratory complications increases dramatically and may become fatal as well [6, 7].

Although there are number of risk factors responsible for bronchiolitis, however, premature birth, immune-deficiencies and

any associated cardio-pulmonary complication are of the commonest determinants [8]. In majority of cases it is caused by viruses, Respiratory Syncytial Virus(RSV) accounts for about 60-75% of all viruses, other viruses involved in causation of bronchiolitis are rhinovirus, influenza and para influenza etc. [9]. The ideal treatment mode is usually supportive. Management through use of corticosteroids and nebulized bronchodilators including ipratropium bromide, salbutamol, and the epinephrine are may also be opted [10]. Salbutamol is a frequently used drug in clinical practice and in complicated cases advanced treatments like use of surfactants and other methods can also be used [11, 12].

Varying dose and administration of saline in nebulization is also proven to give different results in improvement in bronchiolitis [13]. Studies have reported that 3 % hypertonic saline has better health outcomes as reduction in CS score and short duration in terms of stay in the hospital salbutamol nebulization vs the 0.9 % saline group, however, some studies have also reported no significant difference between the two types [14,

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15]. A study reported average stay in the hospital as 3.4 ± 1.7 days vs. 4.9 ± 1.4 days among the patients who were given hypertonic saline was compared to salbutamol with significant mean difference (p -value=0.001). As there is lack of local literature for comparison of the two groups in terms of stay in the hospital [5, 16]. If we also find lower mean hospital stay in HS group then it can be utilized in future to treat the patients. Hence, the rationale of conducting this study is on local population to assess efficacy of the two study groups as mentioned above. Hence, the objective of this study to compare mean hospital stay after nebulization with 3% hypertonic saline Vs salbutamol in treatment of bronchiolitis.

MATERIALS AND METHODS

This study was done at Pediatric medicine ward, Services Hospital using a randomized control trial study design. The study was done during 8th May 2018 to 8th November 2018 (IRB: RTMC/PED-2015-068-3481). A total of 68 cases are estimated i.e. (34 in each group) was taken using average stay at the hospital as 4.9 ± 1.4 days in salbutamol group and 3.4 ± 1.7 days in the Hypertonic Saline group using OpenEpi software, we used 80% power of test and 95% confidence level. The children of age >3 months to < 2 years of both gender and diagnosis of bronchiolitis with no longer than 6 weeks were included. Whilst children with previous wheeze, asthma or any congenital respiratory or cardiac disorders were excluded. Non-probability convenience sampling was used for collection of data which was segregated into two study groups A & B, where A (Salbutamol) and the other was given drug B (Hypertonic Solution) each of which was administered after every 8 hour till discharge. Both treatments were allocated using lottery methods. Dose Salbutamol was taken 0.1mg/kg dilution with distilled water and to obtain 3% Hypertonic Saline 3ml Sodium Chloride 5% mixed with 5cc distilled water. Each two groups received same supportive treatment, sputum aspiration, water electrolyte and oxygen therapy. The outcome variable was hospital stay that was measured from admission to discharge of patients.

STATISTICAL ANALYSIS

Data was analyzed by SPSS software (Version 22). SPSS software was used for data entry and analysis. For quantitative variables like age mean and standard deviation was used whereas for qualitative variables like gender, frequency and percentages were used. Independent sample t-test was used for comparing mean hospital stay among the two groups taking p -value <0.05 as significant and post-stratification for gender, age as well as the duration of the disease.

RESULT

In this study, the average age of the cases in the group who were administered with Salbutamol was 1.06 ± 0.50 years and in Hypertonic solution mean age was 1.24 ± 0.55 years. In patients who were given Salbutamol, 18(52.9%) females, and 16(47.1%) males were present while in Hypertonic solution group there

were 19(55.9%) male and 15(44.1%) female cases. Overall there were 35(51.5%) male and 33(48.5%) female cases with higher male ratio than female. The mean hospital stay in Salbutamol group the mean hospital stay was 4.44 ± 1.08 days while in hypertonic solution the mean hospital stay was 3.18 ± 1.11 days with statistically less mean hospital stay in Hypertonic solution vs the Salbutamol group p -value<0.001.

Moreover, upon stratification for age, in < 1 year of age group the mean hospital stay in Salbutamol group was 4.44 ± 1.09 days and in Hypertonic solution group the average stay at the hospital was 3.17 ± 1.27 with lesser average stay at the hospital in group with Salbutamol (p -value<0.05). In age group of 1-2 years, the mean hospital stay in Salbutamol group was 4.44 ± 1.0 days and in Hypertonic solution group the mean hospital stay was 3.18 ± 1.05 with statistically less mean hospital stay in Hypertonic group p -value<0.05. When data was stratified for gender, male cases the mean hospital stay in Salbutamol group was 4.31 ± 1.20 days and in Hypertonic solution group the mean hospital stay was 3.21 ± 1.18 with statistically less mean hospital stay in Hypertonic group p -value<0.05. In female cases, the mean hospital stay in Salbutamol group was 4.56 ± 0.98 days and in Hypertonic solution group the mean hospital stay was 3.13 ± 1.06 with statistically less mean hospital stay in Hypertonic group (p -value<0.001).

Upon stratification of duration of the disease in cases who had <3 weeks of duration the average stay at the hospital in Salbutamol group was 4.40 ± 1.18 days and in Hypertonic solution group the average stay at the hospital was 3.25 ± 1.14 with statistically less mean hospital stay in Hypertonic group, (p -value<0.001). In cases who had duration of disease 3-6 weeks, the average stay at the hospital in Salbutamol group was 4.47 ± 1.02 days and in Hypertonic solution group the average stay at the hospital was 3.14 ± 1.13 with statistically less average stay at the hospital in Hypertonic group, (p -value<0.001) (Tables 1 and 2).

Table 1. Comparison of Age, Gender and Hospital Stay in Both Study Groups.

		Study Groups		Total	p-value
		Salbutamol	Hypertonic Solution		
Age (years)		1.06 ± 0.5	1.24 ± 0.55	1.15 ± 0.53	0.15
Gender	Male	16(47.1%)	19(55.9%)	35(51.5%)	0.47
	Female	18(52.9%)	15(44.1%)	33(48.5%)	
Hospital Stay (days)		4.44 ± 1.08	3.18 ± 1.11	3.81 ± 1.26	<0.001

Table 2. Comparison of Hospital Stay (Days) in Both Groups with Respect to Age Groups (years), Gender and Duration of Disease.

		Study Groups	Mean	S.D	t-test	P-value
Age (years)	<1 years	Salbutamol	4.44	1.09	2.844	0.009
		HypertonicSolution	3.17	1.27		
	1-2years	Salbutamol	4.44	1.10	3.704	0.001
		HypertonicSolution	3.18	1.05		
Gender	Male	Salbutamol	4.31	1.20	2.733	0.010
		HypertonicSolution	3.21	1.18		
	Female	Salbutamol	4.56	0.98	3.993	<0.001
		HypertonicSolution	3.13	1.06		
Duration of Disease	< 3 weeks	Salbutamol	4.40	1.18	2.552	0.017
		HypertonicSolution	3.25	1.14		
	3-6 weeks	Salbutamol	4.47	1.02	3.961	<0.001
		HypertonicSolution	3.14	1.13		

DISCUSSION

Acute Bronchiolitis is an infection that mostly effects infants and children and is one of the commonest respiratory tract infection associated with significant risk of morbidity as well as mortality [17]. Moreover, it causes a considerable burden on hospital in terms of stay in the hospital and expenditure spent on patient management [9]. Although there could be many reasons for bronchiolitis, one of the most frequently reported reason for this is Respiratory Syncytial Virus (RSV) [18]. Also the pathophysiology and prognosis of the disease is varying, but is characterized by wheezing and hyperinflation mostly [19]. This is because of its effect on bronchiolar epithelium, due to sloughing of epithelial cells, mucus secretions and edema [20]. A number of treatment options including, but not limited to diuretics, corticosteroids and beta-agonists are usually opted but, it may also include Inhaled hypertonic saline (HS) which has recently shown excellent efficacy in treatment of bronchiolitis [21].

Recently studies that have been conducted to see effectiveness of nebulized HS have reported its ability to reduced number of hospital admissions, minimum hospital stay duration and decreased severity of the disease in patients of acute bronchiolitis. Similar results were recently published in a Cochrane Meta-analysis [22, 23]. The average age in this study was 1.15 ± 0.53 years and in group with Salbutamol was 1.06 ± 0.50 years and in Hypertonic solution mean age was 1.24 ± 0.55 years. Recently a study reported mean age in 3% hypertonic saline (HS) as 6.03 ± 3.71 year and in salbutamol group as 5.48 ± 3.35 years. The lesser age in this study may be attributed to the inclusion set for age we took only 3 months to 2 years of age [24].

The average stay at the hospital in this study for group of Salbutamol was 4.44 ± 1.08 days while for the hypertonic solution the average stay at the hospital was 3.18 ± 1.11 days with statistically less mean hospital stay in hypertonic solution vs. the Salbu-

tamol, (p-value<0.001). According to one other study the stay in the hospital was 3.4 ± 1.7 in HS groups and in Salbutamol group the mean hospital stay was 4.9 ± 1.4 days (P=0.001). Hence, 3% HS nebulization was concluded as a safe method to treat moderately ill patients of acute bronchiolitis [24].

Yet one more prospective randomized, double blind study included 3% nebulized HS and other treatment regimens on treatment of acute bronchiolitis and found that both HS and NS groups has significantly lower post treatment Clinical Bronchiolitis Severity Score (CBSS) with p-value<0.001 [25]. Similarly another study reported almost similar average hospital stay in both groups (p-value: 0.747). Also some symptoms such as cough was found 46% vs 20% (P: 0.025) and rhinorrhea 58% vs 31%(P:0.30) were more in HS vs NS groups. Hence, this study did not recommend HS over NS for treatment of acute bronchiolitis [26].

Hence, although few studies report conclusions different from our study, majority are in consensus that 3% HS has significantly greater efficacy against NS for treating the bronchiolitis.

CONCLUSION

This study concludes that the mean hospital stay was comparatively lesser in the patients administered with hypertonic solution compared to the Salbutamol. Moreover, the clinical efficacy of hypertonic saline can be utilized in future to gain early recovery of Bronchiolitis and hence it can reduce the hospital stay and related cost.

AUTHORS' CONTRIBUTION

- **Rabia Nizam and Muhammad Khalid Masood:** Conceptualization of project, Literature search, Data collection, Statistical analysis, Drafting of manuscript, Revision of manuscript.

- **Amna Khalid:** Literature search, Data collection.
- **Mehwish Shafique:** Literature search, Data collection, Statistical analysis, Drafting of manuscript.
- **Mehwish Imtiaz and Shadab Masood:** Literature search, Statistical analysis, Drafting of manuscript.

CONFLICT OF INTEREST

Declared none.

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REFERENCES

- [1] Heppe Montero M, Gil-Prieto R, Walter S, Aleixandre Blanquer F, Gil De Miguel A. Burden of severe bronchiolitis in children up to 2 years of age in Spain from 2012 to 2017. *Hum Vaccine Immunother* 2022; 18(1): 1883379.
- [2] Bem RA, Bont LJ, van Woensel JB. Life-threatening bronchiolitis in children: Eight decades of critical care. *Lancet Respir Med* 2020; 8(2): 142-4.
- [3] Hansen CL, Viboud C, Chaves SS. The use of death certificate data to characterize mortality associated with respiratory syncytial virus, unspecified bronchiolitis, and influenza in the United States, 1999–2018. *J Infect Dis* 2022; 226(Suppl 2): S255-S66.
- [4] Movva N, Suh M, Bylsma LC, Fryzek JP, Nelson CB. Systematic literature review of respiratory syncytial virus laboratory testing practices and incidence in United States infants and children < 5 years of age. *J Infect Dis* 2022; 226(Suppl 2): S213-S24.
- [5] Honcoop AC, Poitevien P, Kerns E, Alverson B, McCulloh RJ. Racial and ethnic disparities in bronchiolitis management in freestanding children's hospitals. *Acad Emerg Med* 2021; 28(9): 1043-50.
- [6] Shi T, Vennard S, Mahdy S, Nair H. Risk factors for RSV associated acute lower respiratory infection poor outcome and mortality in young children: A systematic review and meta-analysis. *J Infect Dis* 2022; 226(Suppl 1): S10-S6.
- [7] Mahant S, Parkin PC, Thavam T, *et al.* Rates in bronchiolitis hospitalization, intensive care unit use, mortality, and costs from 2004 to 2018. *JAMA Pediatr* 2022; 176(3): 270-9.
- [8] Caballero MT, Bianchi AM, Grigaites SD, *et al.* Community mortality due to respiratory syncytial virus in Argentina: Population-based surveillance study. *Clin Infect Dis* 2021; 73(Suppl 3): S210-S7.
- [9] Karron RA. Preventing respiratory syncytial virus (RSV) disease in children. *Science* 2021; 372(6543): 686-7.
- [10] Wopker P, Schwermer M, Sommer S, *et al.* Complementary and alternative medicine in the treatment of acute bronchitis in children: A systematic review. *Complement Ther Med* 2020; 49: 102217.
- [11] Cai Z, Lin Y, Liang J. Efficacy of salbutamol in the treatment of infants with bronchiolitis: A meta-analysis of 13 studies. *Medicine* 2020; 99(4): e18657.
- [12] Buendía JA, Patiño DG. Budget impact analysis of surfactant therapy for bronchiolitis in critically ill infants: The Colombian National Health System perspective. *BMC Health Services Res* 2021; 21(1): 1-8.
- [13] Buendía JA, Acuña-Cordero R. The cost-effectiveness of hypertonic saline inhalations for infant bronchiolitis. *BMC Health Services Res* 2020; 20(1): 1-8.
- [14] Stobbelaar K, Kool M, de Kruijf D, *et al.* Nebulised hypertonic saline in children with bronchiolitis admitted to the paediatric intensive care unit: A retrospective study. *J Paediatr Child Health* 2019; 55(9): 1125-32.
- [15] Heikkilä P, Korppi M. Hypertonic saline in bronchiolitis: An updated meta-analysis. *Arch Dis Child* 2021; 106(1): 102.
- [16] Saleem M, Saleem M, Khurshid A. Hypertonic saline versus normal saline nebulization in hospitalized children with acute bronchiolitis. *Prof Med J* 2020; 27(12): 2734-8.
- [17] Reichert H, Suh M, Jiang X, *et al.* Mortality associated with respiratory syncytial virus, bronchiolitis, and influenza among infants in the United States: A birth cohort study from 1999 to 2018. *J Infect Dis* 2022; 226(Suppl 2): S246-S54.
- [18] Ricci V, Nunes VD, Murphy MS, Cunningham S. Bronchiolitis in children: Summary of NICE guidance. *BMJ* 2015; 350: h2305.
- [19] Hervás D, Reina J, Yañez A, Del Valle J, Figuerola J, Hervás J. Epidemiology of hospitalization for acute bronchiolitis in children: Differences between RSV and non-RSV bronchiolitis. *Eur J Clin Microbiol Infect Dis* 2012; 31(8): 1975-81.
- [20] Mansbach JM, Piedra PA, Teach SJ, *et al.* Prospective multicenter study of viral etiology and hospital length of stay in children with severe bronchiolitis. *Arch Pediatr Adolesc Med* 2012; 166(8): 700-6.
- [21] Rostad CA. Respiratory syncytial virus: Spectrum of clinical manifestations and complications in children. *Pediatr Ann* 2019; 48(9): e349-e53.
- [22] Yu J-F, Zhang Y, Liu Z-B, Wang J, Bai L-P. 3% nebulized hypertonic saline versus normal saline for infants with acute bronchiolitis: A systematic review and meta-analysis of randomized controlled trials. *Medicine* 2022; 101(43): e31270.
- [23] Elliott SA, Gaudet LA, Fernandes RM, *et al.* Comparative efficacy of bronchiolitis interventions in acute care: A network meta-analysis. *Pediatrics* 2021; 147(5): e2020040816.
- [24] Gupta HV, Gupta VV, Kaur G, *et al.* Effectiveness of 3% hyper-

tonic saline nebulization in acute bronchiolitis among Indian children: A quasi-experimental study. *Perspect Clin Res* 2016; 7(2): 88-93.

[25] 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; 24(6): 633-7.

[26] Flores P, Mendes AL, Neto AS. A randomized trial of nebulized 3% hypertonic saline with salbutamol in the treatment of acute bronchiolitis in hospitalized infants. *Pediatr Pulm* 2016; 51(4): 418-25.

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