

# IJMA

## INTERNATIONAL JOURNAL OF MEDICAL ARTS



*Volume 3, Issue 3 [Summer (July-September) 2021]*



<http://ijma.journals.ekb.eg/>

Print ISSN: 2636-4174

Online ISSN: 2682-3780

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- ✓ International Journal of Medical Arts is the Official Journal of the Damietta Faculty of Medicine, Al-Azhar University, Egypt
- ✓ It is an International, Open Access, Double-blind, Peer-reviewed Journal
- ✓ Published four times a year
- ✓ The First Issue was published in July 2019
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## Case Report

# Efficacy of Nebulized Hypertonic Saline 3% in comparison to Nebulized Normal Saline 0.9% in Children with Acute Bronchiolitis

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Submission date: September 09, 2020; Revision date: May 25, 2021; Acceptance date: May 26, 2021



DOAJ

DOI: [10.21608/IJMA.2021.42037.1162](https://doi.org/10.21608/IJMA.2021.42037.1162)

## ABSTRACT

**Background:** Bronchiolitis is the most common lower respiratory tract infection in children. The management guidelines recommend only supportive measures; however, there is an increasing burden for bronchiolitis especially in developing countries. The use of nebulized hypertonic saline may aid in decreasing hospital stay and decrease the global burden of the disease.

**Objective:** To compare between the efficacy of hypertonic saline versus normal saline in reducing duration of hospital admission and improving symptoms of acute bronchiolitis.

**Patients and methods:** A randomized comparative clinical trial included 90 children with acute bronchiolitis, conducted at Al-Azhar University Hospital [New Damietta] during the period from October 2019 till June 2020. Patients were randomly assigned into 2 groups; 45 patients received 3% hypertonic saline nebulization [group 1], and 45 patients received 0.9% normal saline nebulization [group 2]. Efficacy of treatment was assessed through duration of hospitalization and oxygen supplementation, and severity of respiratory distress.

**Results:** there was no significant difference between both groups as regard to age, sex, baseline clinical severity score and O<sub>2</sub> saturation. After treatment, patients who received nebulized hypertonic saline showed less duration of hospitalization [62.3±20.8 hours vs 76.8± 26.1 hours; p=0.001], less duration of O<sub>2</sub> therapy [16.2±6.0 hours vs 25.3±5.4 hours; p=0.01]. As regard to severity clinical score, patients received nebulized hypertonic saline showed significant improvement started within 24 hours from admission [P=<0.001].

**Conclusions:** Nebulized hypertonic 3% saline is effective in reducing hospital stay among children with bronchiolitis compared with nebulized normal saline. Further large studies are required to confirm these results.

**Keywords:** Nebulization; Bronchiolitis; Normal saline; Hypertonic saline.

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**Citation:** Elesh HM, El Khaleegy HA, Elsamanoudy MI. Efficacy of Nebulized Hypertonic Saline 3% in comparison to Nebulized Normal Saline 0.9% in Children with Acute Bronchiolitis. IJMA 2021; 3 [3] July-September: 1584-1588 [DOI: 10.21608/IJMA.2021.42037.1162].

\* Main subject and any subcategories have been classified according to the research topic.

## INTRODUCTION

Acute bronchiolitis is a common viral infection of the lower respiratory tract in infants and young children. The causative organism in the majority of cases is respiratory syncytial virus. The duration of illness is usually 4 to 7 days, but prolonged cough may occur in many children [1]. There are no effective treatments for bronchiolitis. Hospital admission may be needed either for support of feeding or for the treatment of hypoxia. Sometimes, intensive care is required if respiratory failure had occurred [2].

Oxygen therapy for infants with bronchiolitis reduced mortality rates significantly; however, bronchiolitis remains one of the major causes of infant mortality [3]. In spite of the presentation of many lines of therapy, including oxygen therapy, antiviral drugs, oral and nebulized corticosteroids and a diversity of bronchodilators, these agents have neither decreased length of inpatient ward stay nor impacted the course of the acute illness [4].

Over the past decade, many studies have recommended the use of nebulized hypertonic saline to diminish the duration of the illness and, subsequently the duration of hospitalization [5-7]. It has been suggested that hypertonic saline might diminish the viscidness of bronchial secretions, lowers airway edema, and recover the process of mucus clearing by cilia. In addition, hypertonic saline beneficially modifies the process of mucus clearance by cilia in both normal and unhealthy lungs [8].

## AIM OF THE WORK

The aim of the present study is to compare the effectiveness of hypertonic saline against normal saline in reducing the duration of hospital admission, need for oxygen supplementation and improving symptoms of acute bronchiolitis.

## PATIENTS AND METHODS

The study is a randomized prospective comparative clinical trial that was conducted at the inpatient ward of "pediatric department of Al-Azhar University Hospital [New Damietta]". The study was conducted during the period from October 2019 through June 2020. Infants aged 1-24 months presenting with symptoms and signs matched with the diagnosis of bronchiolitis, and requiring hospitalization were included in the study. Acute bronchiolitis was diagnosed according to the "American Academy of Pediatrics guidelines as a constellation of clinical signs and symptoms occurring in children younger than 2 years, including viral upper respiratory tract prodrome [cough or rhinitis], followed by tachypnea, wheezing, rales, use of

accessory muscles and nasal flaring" [9]. The decision for hospitalization was based on the guidelines of "National Institute for Health and Care Excellence" [10], if the patient has any of the following: apnea, persistent oxygen saturation of < 92% on room air, insufficient oral fluid consumption [50%-75% of typical volume], and persisting critical respiratory distress.

Exclusion criteria were family history of asthma, history of atopic diseases, history of prematurity, presence of chronic diseases [pulmonary, cardiac or neurological], more severe disease requiring mechanical ventilation, use of steroids or bronchodilators before hospitalization, and radiological evidence of pneumonia.

Patients were randomly assigned to one of two groups; 45 patients received 3% hypertonic saline nebulization [group 1], and 45 patients received 0.9% normal saline nebulization [group 2]. Each child enrolled in the study was subjected to careful history, including a history of similar attacks, family history of asthma and atopies. A complete physical examination was performed. Chest X-ray was done to exclude pneumonia. Treatment was implemented according to the guidelines of "National Institute for Health and Care Excellence" [10]. The protocol involved the avoidance of physical therapy, antibiotics, bronchodilators and corticosteroids. Oxygen supplementation was given if the oxygen saturation is persistently less than 92%. Oxygen saturation was measured and recorded at admission using noninvasive pulse oximeter. Oxygen therapy was stopped when the patient-maintained O<sub>2</sub> saturation > 95% in room air. Suctioning of the upper airway was considered in patients who have respiratory distress or experienced significant feeding difficulties because of nasal secretions, or had a significant apnea, even in the absence of nasal secretions. Fluids were given by naso-gastric or oro-gastric tubes in children when oral fluid ingestion was not sufficient. Intravenous isotonic fluids were given in patients intolerable to nasogastric or oro-gastric fluids or have imminent respiratory failure. In addition to the previous treatments, each patient received nebulization four times every day at intervals of 6 h according to the following schedule until discharge [11]: group 1 [hypertonic saline group]: obtained 4 ml of nebulized 3% hypertonic saline; and group 2 [normal saline group]: obtained 4 ml of nebulized 0.9% normal saline. All nebulization were supplied to infants through air-compressed nebulizers. Discharge of patients was done according to guidelines of "National Institute for Health and Care Excellence" [10] as follows: the patient is clinically stable, the patient is taking adequate oral fluids, and the patient has preserved oxygen saturation more than 92% on room air for 4 h, containing a time of sleep.



The primary outcome measure was the duration of hospitalization. It was stated as the time from enrollment in the study till the child is candidate for discharge as determined by the responsible physician. The secondary outcome measures were 1] duration of oxygen supplementation: total duration since the beginning of supplying oxygen until the removal of oxygen supply, 2] the severity of respiratory distress: through repeated evaluation [every 12 h] by respiratory distress assessment instrument [RDAI] [12] score [Table 1] till discharge, and 3] drug side effects: There were no reported side effects or changes in color, smell, or other physical properties among both groups.

**Ethical consideration:** Informed consent was obtained from parents of the patients being studied for participation in the study. The approval of Institutional Review Board [IRB] was obtained.

**Statistical analysis:** The collected data were analyzed using statistical package for social sciences version 19 [SPSS Inc, Chicago, USA], running on IBM compatible computer. Testing for normal distribution was done by Kolmogorov–Smirnov and Shapiro–Wilk tests. For comparison between two groups, independent samples [t] test or Mann–Whitney tests were used. For comparison between categorical groups, the Chi square [X<sup>2</sup>] test was used. For all tests, P values < 0.05 were considered statistically significant [13].

**Table [1]: "Respiratory distress assessment instrument" [12]**

Variables	0	1	2	3
Respiratory rate	<30b/m	31 to 45 b/m	46 to 60 b/m	>60 b/m
Wheezing	None	Terminal expiratory or only with a stethoscope	Entire expiration or audible on expiration without a stethoscope	Inspiration and expiration without a stethoscope
Retraction	None	Intercostals only	Tracheosternal	Severe with nasal flaring.
General condition	Normal			Irritable, lethargic, or poor feeding

\*: "A value is assigned for each variable and higher scores indicate a worst respiratory condition"

## RESULTS

There was no significant difference between both groups as regard age, sex and clinical severity at admission [table 2]. After treatment, group 1 showed marked improvement of clinical severity score started from 12 h from admission [8.1 in group 1 vs. 9.1 in group 2; P=0.03], and continued up to 72 h [figure 1]. Finally, patients who received nebulized hypertonic saline showed less duration of hospitalization [62.3±20.8 h vs. 76.8± 26.1 h; p=0.001] and less duration of O<sub>2</sub> therapy [16.2±6.0 h vs. 25.3±5.4 h; p=0.01] as shown in table [3].

**Table [2]: General characteristics and clinical presentation of the cases on admission**

	Group-I [n = 45]	Group-II [n = 45]	p-value
Age [months] Mean ± SD	5.3 ± 2.81	5.1 ± 2.62	0.750
Age [months]			0.758
– < 6	27 [60%]	25 [55.6%]	
– 6-12	15 [33.3%]	16 [35.6%]	
– >12	3 [6.7%]	4 [8.9%]	
Sex			0.761
Male	24 [53.3%]	25 [55.6%]	
Female	21 [46.7%]	20 [44.4%]	
Running nose	45 [100%]	45 [100%]	1
Cough	45 [100%]	45 [100%]	1
Wheeze	40 [88.8%]	42 [93.3%]	0.321
Feeding difficulty	24 [53.3%]	25 [55.6%]	0.215
Nasal flaring	7 [15.6%]	9 [20%]	0.423
Tachypnea	40 [88.8%]	38 [84.4%]	0.315
Tachycardia	40 [88.8%]	38 [84.4%]	0.315
Rhonchi	45 [100%]	45 [100%]	1
Fever	12 [26.66%]	11 [24.4%]	0.217
Oxygen saturation (mean± SD)	94.8 ±10.6	94.4 ±11.2	0.721

**Table [3]: Comparison of primary and secondary outcomes between both groups**

	Group-I [n = 45]	Group-II [n = 45]	p-value
Length of hospitalization [hours]	62.3 ± 20.8	76.8± 26.1	0.001*
Rapid discharge [within 72 hours]	40 [88.9]	28 [62.2]	0.01*
Patients required O <sub>2</sub> supplement	8 [17.7%]	15 [33.3%]	0.14
The duration of O <sub>2</sub> supplement [hours]	16.2±6.0	25.3±5.4	0.01*

\*: significant

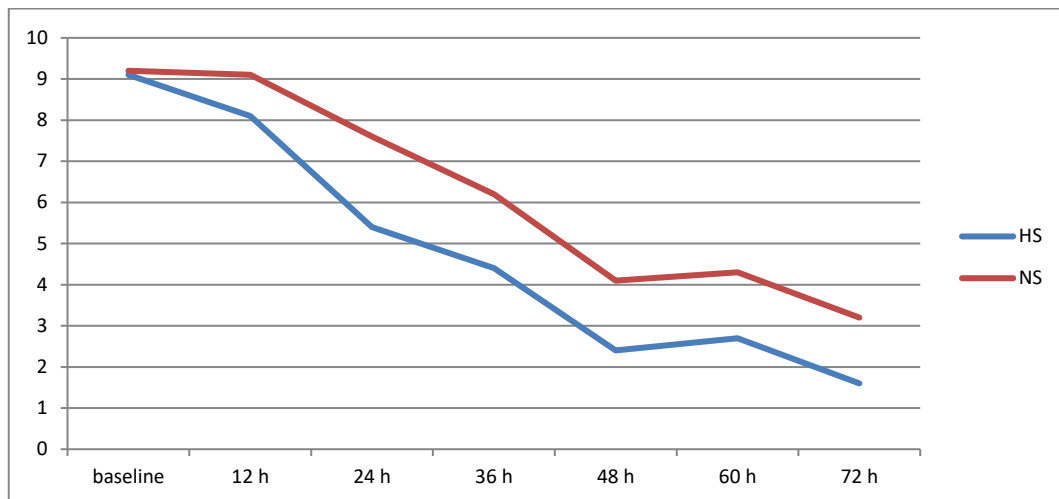


Figure [1]: Comparison of RADL score at admission and every 12 hours over 3 days

## DISCUSSION

Acute viral bronchiolitis is regarded as a common disease in children from birth till the age of two years as it is the mainly recognizable cause of respiratory infection during early childhood [14]. This study has been conducted to investigate whether the 3% nebulized hypertonic saline can reduce the severity of the clinical course and the length of hospitalization period in bronchiolitis patients than nebulized normal saline performs. In this study, the two study groups were nearly similar as regard to their demographic characteristics, such as baseline clinical characteristics, age and sex, RADL score and oxygen saturation on breathing room air.

The study showed that the two groups of children had the same pertinent baseline clinical characteristics; thus, the outcome differences between the studied groups [improved among 3% nebulized hypertonic saline group] can be accredited to interference. In addition, respiratory rate score of both groups were decreased and the level of O<sub>2</sub> saturation on breathing room air was better after 72 h being much earlier in the 3% nebulized hypertonic saline group. In the present study, none of the children suffered from any side-effects. In cases where O<sub>2</sub> saturation drops constantly less than 90%, the patient with bronchiolitis should receive oxygen supplementation, which may be withdrawn when O<sub>2</sub> saturation is at or more than 95% if the infant is well-fed and has no or negligible respiratory distress [15]. In the hypertonic saline group, the average duration of oxygen supply was significantly reduced than that in the normal saline group. About 88.9% of the children in the hypertonic saline group improved within 72 h, while about 62% of the children of the 0.9% saline group recovered within the same period. Similar findings were shown by Martin *et al.* [16].

The present study demonstrated that 3% hypertonic saline caused a significant reduction in the duration of hospitalization. The majority of patients received hypertonic saline were recovered and left the hospital within 3 days of treatment. The same has been observed in 2 studies, where the mean duration of hospitalization was shorter in the hypertonic saline group [17, 18]. Several investigators have reported consistent findings to the present study in regards of the use of hypertonic saline solution in infants with bronchiolitis in addition to substantial benefits of therapy reported by them [19, 20]. These studies found that nebulized hypertonic saline decreases the length of hospital stay in comparison with normal saline among hospitalized infants.

A recent review of eleven randomized clinical trials, including infants with acute bronchiolitis, both inpatients and outpatients, concluded that nebulized 3% saline might cause a significant reduction in the length of hospitalization and enhance the clinical severity score [8]. In contrast, a conventional finding was found by another small trial that carried out in the emergency department setting, and the investigators reported that immediate clinical benefits may not be seen with nebulized hypertonic saline [21].

The predominant pathological features in acute viral bronchiolitis are airway edema and mucus plugging. Hypertonic saline decreases airway edema, improves mucus rheological properties and mucociliary clearance, and as a result, it decreases airway obstruction. It is believed that hypertonic saline helps in the elimination of inspissated secretions through disturbance of mucus filament crosslinking and decrease of mucosal edema [8, 22].

This study showed that the two study groups exhibited evident clinical recovery and improvement in oxygen

saturation, yet, 3% hypertonic saline group is more efficient in improving oxygenation, relieving symptoms, and reduction in the length of hospital stay in infants with acute bronchiolitis in comparison with the 0.9% normal saline group. It appears that the treatment with nebulized hypertonic saline in hospitalized children with bronchiolitis is a harmless and effective method. This policy has great potential for cost saving as it is a cheap intervention, especially in developing countries, as it reduces the duration of hospitalization as demonstrated in the present study.

**Conclusion:** Nebulized hypertonic 3% saline is effective in reducing hospital stay among children with bronchiolitis compared with nebulized normal saline. Further large-scale studies are needed to confirm these results.

#### Financial and Conflict of interest disclosure

"Authors declare no conflict of interest"

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# International Journal



<https://ijma.journals.ekb.eg/>

Print ISSN: 2636-4174

Online ISSN: 2682-3780

# of Medical Arts