

**HOSPITAL ADMISSIONS AFTER STANDARD AND POSITIVE PRESSURE NEBULIZATION IN  
PATIENTS WITH BRONCHIOLITIS**

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## **ABSTRACT**

**Background and Significance:** In the United States, bronchiolitis has consistently been the most common diagnosis leading to hospitalization in infants under one year of age, representing over 90,000 cases a year and a significant financial burden on the healthcare system. A condition with such widespread incidence should have an established algorithm for treatment of respiratory symptoms, but studies on the efficacy of certain therapies have been inconclusive. Some reports suggest that the use of positive pressure nebulization may be of benefit in treating bronchiolitis, but it has not yet been studied systematically.

### **Research Question and Objectives:**

- 1) To determine whether positive pressure nebulization (PPN) is more effective than standard nebulization (SN) in reducing admission rate in infants with bronchiolitis
- 2) To determine whether the use of positive pressure nebulization causes a change in Bronchiolitis Score, Pediatric Intensive Care Unit (PICU) admission rate, length of stay (LOS), and unscheduled returns to the pediatric emergency department (PED)

**Methods:** The project is a retrospective study conducted at a single-center tertiary care children's hospital. Participants included in the study were infants 2-24 months of age with moderate to severe bronchiolitis, who were evaluated by trained respiratory therapists using an objective scoring tool and treatment algorithm that included suctioning, albuterol, and racemic epinephrine. Infants received the above nebulization therapies by either a standard or a positive pressure nebulization delivery device. The two treatment groups were compared to see if one approach was superior as measured by outcomes such as hospital and PICU admission rate, length of stay, and returns to the emergency department.

**Results:** Initial survey of the 2012-2013 winter season at Phoenix Children's Hospital yielded 2,095 patients who were diagnosed with bronchiolitis. As the majority of patients were excluded due to age, comorbidities, or poor documentation of treatment, our study examined 19 patients who received positive pressure nebulization, which were matched in a 1:3 ratio

(PPN:SN), for a total of 57 patients who received standard nebulization. In measuring the primary markers of outcome, we found that 12 of the 19 PPN patients (63%) were admitted to the regular pediatric ward, and 4 of the 19 (21%) were admitted to the PICU. 35 of the 57 SN patients (63%) were admitted to the regular pediatric ward, and 5 of the 57 (8%) were admitted to the PICU. Statistical analysis showed that the estimated minimum 'n' required in each treatment group was 252 patients, but our study was only able to obtain a sample size of 19 patients in the PPN group, which was not enough for statistical significance.

**Conclusion:** An association between hospital admission rate with positive pressure nebulization or standard nebulization was not able to be determined.

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## INTRODUCTION & SIGNIFICANCE

### *Background and Rationale*

Bronchiolitis is a lower respiratory tract infection syndrome that can be caused by a variety of different viruses. 50-80% of bronchiolitis cases occur due to infection by RSV, while other cases can be caused by influenza virus, parainfluenza virus, or human metapneumovirus. In the case with RSV, the virus first enters through the *upper* respiratory tract and spreads to the *lower* respiratory tract within a matter of days, resulting in respiratory changes and symptoms that could eventually progress to bronchiolitis that often requires hospitalization. Such changes include: inflammation of bronchiolar epithelia, infiltration of WBC into the bronchioles, edema of the respiratory mucosa, and eventually partial or total airway obstruction due to necrotic epithelium, fibrin deposition, or excess production of mucus.

As bronchiolitis is the most common diagnosis among hospitalized infants under a year of age in the United States, the financial implications of this condition can not be ignored. With about 90,000 hospitalizations annually in the US alone just within this age group, over \$700 million goes into caring for and treating these children in a hospital setting.

As some of the hallmarks of bronchiolitis include inflammation and edema of the airways that target the lower respiratory tract, it seems that treatment with an alpha and beta agonist would ameliorate these symptoms. Stimulation of the alpha-receptors would reduce capillary leakage via vasoconstriction of the bronchial arterioles that funnel into the capillary beds, thereby decreasing hydrostatic pressure and reducing edema. Stimulation of the beta-receptors would directly dilate the bronchioles to allow for more patent airways and better oxygenation. In theory, these receptors represent a therapeutic target for intervention. However, studies have not shown a conclusive algorithm with clinically significant results, thus presenting an opportunity to improve care for such a common diagnosis.

### *Current Guidelines for Treatment*

Currently, there are a number of studies that have examined the efficacy of particular treatment modalities, but the variation in the treatment itself, hospitalization rates, and length of stay in the hospital points to a lack of consensus and an opportunity to improve care for this common syndrome. One study that compared standard epinephrine nebulization to placebo in infants with acute bronchiolitis showed that nebulized epinephrine did not decrease the infant's length of stay in the hospital nor improve clinical status<sup>23</sup>. Yet another study showed that hospitalized infants younger than 18 months of age who were diagnosed with acute bronchiolitis actually did show an improvement of oxygen saturation and clinical signs after nebulized epinephrine therapy<sup>16</sup>. The primary agent in question is racemic epinephrine, a mixture of the levorotatory and dextrorotatory forms of epinephrine which is thought to have a therapeutic advantage over levorotatory epinephrine alone.

In 2014, the AAP released updated bronchiolitis treatment guidelines as an effort to standardize care of these infants with bronchiolitis that required hospitalization. Some noteworthy recommendations include:

- 1) Bronchodilators should not be routinely used for management of bronchiolitis. Many of the positive studies of bronchodilators in the treatment of bronchiolitis have only shown a brief improvement that has an unclear significance clinically
- 2) Supplemental oxygen and continuous monitoring are not routinely recommended unless oxyhemoglobin saturation (SpO<sub>2</sub>) falls below 90%. At that point, supplemental oxygen should be used to maintain SpO<sub>2</sub> levels at 90% or greater. Evaluation of the infant's clinical work of breathing can also drive a provider's decision to use supplemental oxygen.

With regard to bronchiolitis outcomes, pulse oximetry (hypoxia) is considered to be the variable most strongly correlated with hospitalization. Low arterial blood oxygen level (hypoxemia) is the most common cause for hospitalization and clinically serves as an indication of pulmonary ventilation-to-perfusion mismatch that occurs due to inflammatory obstruction of small airways as well as deflation of the alveoli (atelectasis).

### *Research Questions*

- 1. To determine whether positive pressure nebulization is more effective than standard nebulization in reducing admission rate in infants with bronchiolitis*

We hypothesize that positive pressure nebulization will reduce admission rate in infants diagnosed with moderate to severe bronchiolitis when compared to standard nebulization techniques.

- 2. To determine whether use of positive pressure nebulization causes a change in: Bronchiolitis Score, Pediatric Intensive Care Unit (PICU) admission rate, length of stay (LOS), and unscheduled returns to the pediatric emergency department (PED).*

We hypothesize that positive pressure nebulization will produce a positive change in the parameters listed above, which are all markers for determining the efficacy of treatment. For example, a decreased LOS in the hospital and fewer unscheduled returns to the PED (along with changes in the other parameters) would provide evidence for positive pressure nebulization being a superior treatment modality compared to standard nebulization.

While various treatment modalities have been investigated as a potential therapy for bronchiolitis, none have yielded a definitive benefit. As a sequential treatment protocol is in place that was set forth by the American Academy of Pediatrics (AAP), this study aims to show if

positive pressure nebulization can demonstrate a clear benefit over standard nebulization for potential re-evaluation of bronchiolitis treatment guidelines.

### *Goals for the Study*

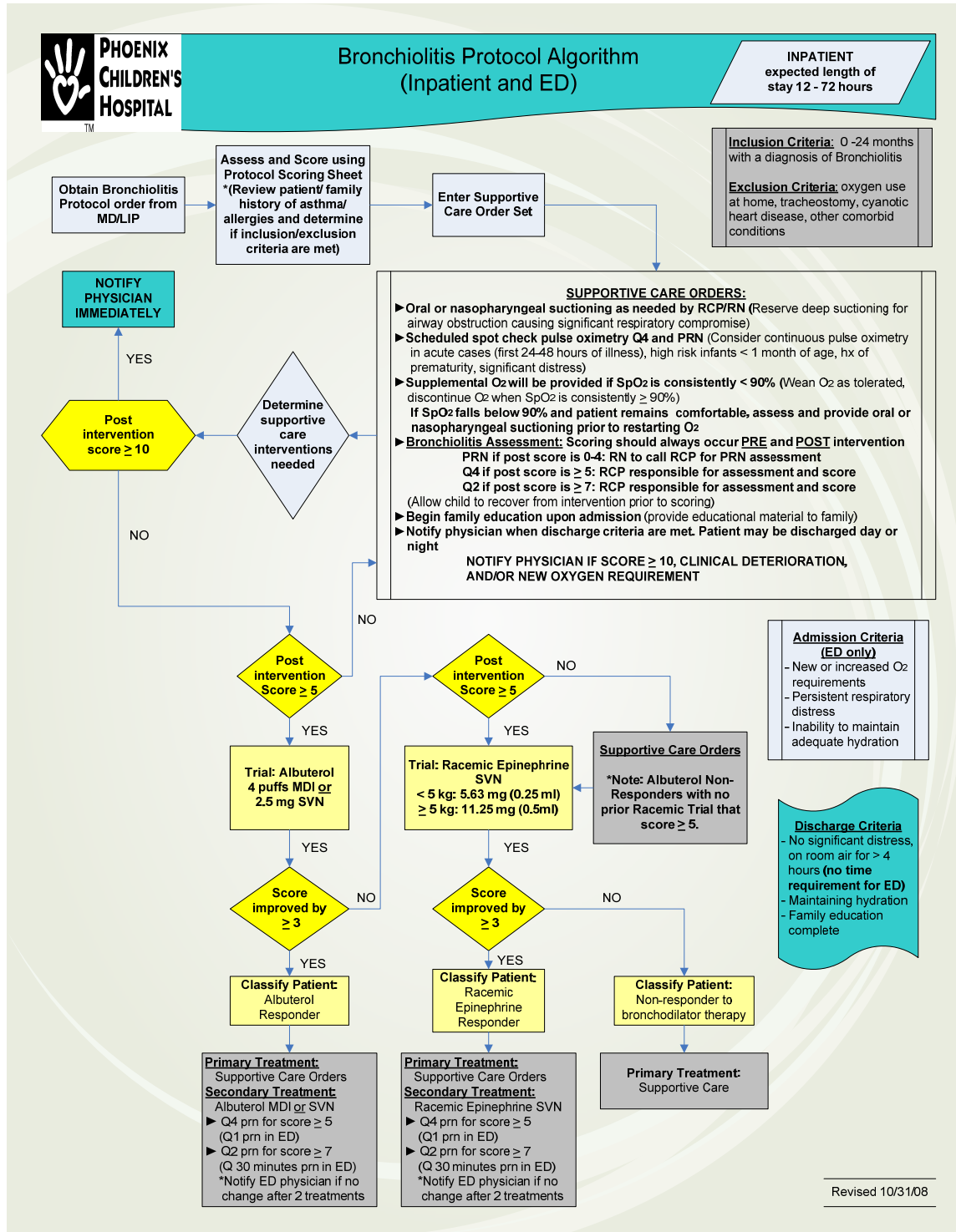
Recently, trials of large populations have produced contradictory findings with regard to the efficacy of either bronchodilators or corticosteroids in treating bronchiolitis. Overall, the current evidence corroborates the AAP recommendation that advises against the routine use of bronchodilators for symptomatic management of bronchiolitis. However, these studies show that a closely monitored trial of bronchodilator therapy can be a reasonable option in a select group of patients, with its continuation dependent upon a documented beneficial response. With regard to improving oxygenation, studies to investigate optimal oxygen delivery methods aimed at reducing ventilation-to-perfusion mismatch and atelectasis have not yet been done. Our study will serve to evaluate whether using a newly developed positive pressure nebulization device improves oxygenation by reducing this mismatch and atelectasis, to decrease hospitalization in infants diagnosed with moderate to severe bronchiolitis.

## **MATERIALS AND METHODS**

### *Preliminary Information and Data*

Considering the ambiguity of efficacious management of bronchiolitis today, a team at Phoenix Children's Hospital developed a comprehensive Bronchiolitis Protocol Algorithm for inpatient and ED care in order to minimize variation and improve clinical outcomes (see Figure 1). Taking into account the recommendations set form by the AAP, this algorithm lays out the step-wise management of infants diagnosed with bronchiolitis. The sub-group that the algorithm outlines care for includes infants of ages 0-24 months with a diagnosis of bronchiolitis. As mentioned above, exclusion criteria include home oxygen use, tracheostomy, cyanotic heart disease, as well as other comorbid respiratory conditions.

**Figure 1: Phoenix Children's Hospital Bronchiolitis Protocol Algorithm**



Patients were evaluated using an objective scoring system (see Figure 2). Infants with higher respiratory distress scores were treated in a step-wise manner beginning with (1) suctioning, (2) albuterol nebulizer, and/or (3) racemic epinephrine. After each intervention was delivered, infants were re-evaluated for their response to the given therapies and given a second respiratory distress score. If it was determined that the therapy was of benefit (measured by improvement in score), that particular intervention was continued. If there was no improvement, the next therapeutic measure in the sequence was considered. If there was still no improvement with the three aforementioned therapies, these patients were treated at the discretion of the healthcare provider, via heated humidified nasal cannula (HHNC) or intubation, both of which require admission to the PICU.

**Figure 2: Bronchiolitis Pathway Scoring and Patient Classification Sheet**

**Bronchiolitis Scoring System:**

	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>
<b>Respiratory Rate</b>	0-6 mo < 50 6mo – 1yr < 40 1 yr+ < 30	0-6 mo < 60 6mo – 1yr < 50 1 yr+ < 45	0-6 mo < 70 6mo – 1yr < 60 1 yr+ < 60	0-6 mo > 70 6mo – 1yr > 60 1 yr+ > 60
<b>SaO<sub>2</sub></b>	≥ 90 %	> 88 %	> 86 %	≤ 85 %
<b>General Appearance</b>	Calm No distress	Mildly irritable; easy to console	Moderately irritable; difficult to console	Extremely irritable; cannot be comforted
<b>Retractions and nasal flaring (NF, SS, IC, SC)</b>	None	1 of 4	2 of 4	3 or more
<b>Auscultation</b>	Clear	Scattered wheezes	Diffuse expiratory wheezing	Biphasic wheezing or very poor air movement

**Classification System:**

Scores	Trial: Albuterol		Trial: Rac Epinephrine	
	Pre SVN	Post SVN	Pre SVN	Post SVN
Respiratory Rate				
SaO <sub>2</sub>				
General Appearance				
Retractions				
Auscultation				
<b>Total Score</b>				
<b>Responder (Yes / No)</b>				

**Summary of Patient Classification:**

- Patient responds to Albuterol
- Patient responds to Racemic Epinephrine
- Patient does not respond to bronchodilator therapy

It should be noted that positive pressure nebulization is an adaptation of a previously existing modality and is currently in use at PCH. The PCH ED shifted from use of regular nebulization to positive pressure nebulization in the winter viral season of 2012 to 2013. Positive pressure nebulization is hypothesized to improve oxygenation via decreasing atelectasis. Again, use of positive pressure nebulization has not been studied systematically in patients diagnosed with moderate to severe bronchiolitis, so this study serves to investigate a potential therapeutic benefit of positive pressure nebulization in improving outcomes.

### *Methodological Approach*

This study followed the treatment outcomes in two groups – positive pressure nebulization and standard nebulization. Though hospital admission rate is the study's primary gauge of treatment outcome, secondary markers of outcome analyzed were bronchiolitis score, length of stay, and unscheduled returns to the pediatric emergency department.

### *Exclusions from the Study*

Generally speaking, bronchiolitis is considered to be a benign process with relatively low morbidity and mortality. There are however, groups at increased risk of developing complications from bronchiolitis.

Among these, apnea is an important consideration in young infants specifically with RSV-associated bronchiolitis. A retrospective study of 691 infants under 6 months of age who were hospitalized for bronchiolitis revealed that apnea occurred in 19 patients (2.7%). All of these apneic infants were identified by risk criteria that included either (1) a history of an apneic episode having already occurred or (2) young age, defined as less than 1 month for term infants or a post-conceptual age of 48 weeks for premature infants. Therefore, infants less than 2 months, or 48 weeks post-conceptual age, will be excluded from the study.

Another high-risk group that will be excluded from the study are patients with underlying complex respiratory comorbidities such as home oxygen use, tracheostomy, or cyanotic heart disease.

Young age and comorbid conditions represent high-risk groups as well as the second and third most common reasons for hospital admission for bronchiolitis. By excluding these groups from the study, we can rule out reasons why otherwise healthy infants are admitted for moderate to severe bronchiolitis.

### *Study Population and Design*

To determine whether positive pressure nebulization yields a greater therapeutic effect compared to standard nebulization, this study investigates any variability in the following parameters to determine one treatment's superiority over the other: bronchiolitis score, pediatric intensive care unit admission, length of stay, and unscheduled returns to the pediatric emergency department.

Infants between the ages of 2-24 months diagnosed with clinical bronchiolitis (defined by viral-associated wheezing) during the winter season of 2012-2013 were first assessed and scored using a Protocol Scoring Sheet that included a patient or family history of asthma or allergies. If patients had any of the respiratory comorbidities described above, they were excluded from this study. A review of Phoenix Children's Hospital's electronic medical record for the ICD codes for the diagnosis of bronchiolitis then allowed us to identify a sub-group for analysis. For infants who had achieved a moderate to severe score on the Protocol Scoring Sheet, suctioning was the first therapy, followed by inhalation therapy for those who failed to respond to suctioning. As the standard of care for viral-associated bronchiolitis shifted from regular nebulization to positive pressure nebulization during this winter season of 2012 to 2013, results were compared from that season to the previous season. In these months, there are at least 2 respiratory therapists assigned to the ED. At the discretion of the physician, viral

nasopharyngeal swabs were collected, and this study will track the viral etiology to categorize them based on outcome.

### *Conduct*

Under the supervision of my mentor, I reviewed the charts of enrolled patients to analyze the primary outcome of hospital admission rate as well as the primary reason for admission using a standardized data collection. In order, the most common reasons for admission for bronchiolitis are hypoxia, young age, and comorbid conditions, with the latter two being excluded from this study. This subgroup analysis for reasons of admission is crucial in showing the positive pressure nebulizer's potential effect on reducing admission rates.

To address the secondary markers of outcomes, the change in bronchiolitis score was measured using a numerical scale from 0-15, with 15 being the most critically ill patients. An assessment of hypoxia was defined to be oxygen saturations less than 90%. The length of stay was measured in hours. Unscheduled returns to the emergency department with the same diagnosis were defined as those occurring within 7 days of initial discharge. We also tracked any admissions to the Pediatric Intensive Care Unit. And lastly, we tracked the reason for admission, specifically looking at hypoxia, dehydration where intravenous fluids were required, and respiratory distress.

## **RESULTS**

In the winter season of 2012-2013, a total of 2,095 patients were diagnosed with bronchiolitis at Phoenix Children's Hospital. It is unclear the exact proportion of patients who had received standard versus positive pressure nebulization due to poor documentation that led to the uncertainty of the patient actually receiving positive pressure nebulization. Only 19 patients who received positive pressure nebulization were included in the study. The rest were excluded due to age, comorbidities, the poor documentation as described above, and delayed timing of administration (receiving positive pressure nebulization after admission to the floor or PICU). The 19 positive pressure nebulization patients were randomly matched according to their age, in a 1:3 (PPN:SN) ratio, for a total of 57 standard nebulization patients.

In measuring the primary markers of outcome, we found that 12 of the 19 PPN patients (63%) were admitted to the regular pediatric ward, and 4 of the 19 (21%) were admitted to the PICU. 35 of the 57 SN patients (63%) were admitted to the regular pediatric ward, and 5 of the 57 (8%) were admitted to the PICU.

To track the reason for admission, 11 of the 19 PPN patients (58%) were admitted for persistent hypoxia, 4 of the 19 (21%) for dehydration, and 4 of the 19 (21%) for persistent respiratory distress. 17 of the 57 SN patients (30%) were admitted for persistent hypoxia, 12 of the 57 (21%) for respiratory distress, and 17 of the 57 (30%) for both reasons. 11 of the 57 (19%) were admitted for other unspecified reasons. No SN patients were admitted for dehydration. Of both groups, only one patient (in the PPN group) returned to the pediatric emergency department with the same diagnosis of bronchiolitis within 7 days of discharge.

In order to assist with estimation of an assumed baseline admission rate, we looked at the first quarters of 2008 and 2009 (which represent peak respiratory season), in which there were a total of 1,088 and 1,064 patients, respectively. Admission rates over the respective two

years at PCH were 40.5% and 37.2%, with an average of 38.9%. As stated before, the primary measure of outcome in this study is admission rate. Taking into account sample size and power, our study assumes a baseline admission rate of 40%, and we aimed to achieve a change of 20% in admission rate. Using a 2-tailed chi-square analysis with an alpha of 0.05 and a beta of 0.8, the estimated minimum 'n' required in each group was 252 patients. However, we were only able to obtain a sample size of 19 patients in the PPN group, which was not enough for statistical significance.

## **DISCUSSION**

For a condition of such high incidence in the United States, there are few treatment modalities that provide a consistent therapeutic benefit for infants with severe to moderate bronchiolitis. Studies have shown that children under the age of two who have previously been hospitalized for bronchiolitis (specifically RSV-related) are at higher risk of developing asthma or wheezing later on in childhood. So far, no study has been performed that compares positive pressure nebulization to standard nebulization with regard to hospital admission rates. Our results showed that the admission rate to the pediatric floor was the same in both groups. However, a smaller percentage of patients was admitted to the Pediatric Intensive Care Unit from the standard nebulization group.

The most common reason for admission in both groups was hypoxia. There were a number of significant limitations to our study. The small sample size led to the inability to produce statistically significant results and was likely due to poor documentation of administration of positive pressure nebulization by physicians and respiratory therapists. Review of the billing records showed that more patients received positive pressure nebulization than actually documented, but they could not be included in the study. Though the patients in each group were matched based on age, exact matches could not be made. Further studies need to be conducted to examine the effect and potential benefit of positive pressure nebulization in improving outcomes in infants with bronchiolitis.

## **FUTURE DIRECTIONS**

As some of the limitations to our study were outlined above, we recognize that there is still a lot of information to be discovered about the various treatment modalities in treating viral bronchiolitis in this infant population, especially considering the lack of systematic studies regarding the potential benefit of positive pressure nebulization.

If indeed positive pressure nebulization proves to be superior to standard nebulization with regard to reducing hospital admission in infants with bronchiolitis, another branch of the study could entail investigating the timing of administration after initial presentation to the emergency department. This would allow us to identify the time window when treatment appears to be the most effective - and perhaps we could even uncover a role for prophylactic administration of positive pressure nebulization before V/Q mismatch and atelectasis occurs in these infants.

If such a study were to be conducted, the importance of accurate timely documentation should be stressed, so that it can clearly be elucidated the type of treatment each patient received. As our study employed a 1:3 PPN:SN matched ratio, any future study would achieve a better chance of statistical significance if the number of patients was equally matched for both groups.

## **CONCLUSIONS**

Considering how common the diagnosis of bronchiolitis is in infants, it is surprising that a widely accepted, established regimen for symptom management does not exist. There has been anecdotal evidence that positive pressure nebulization in these infants can be beneficial, but it has never been systematically studied to date. As hypoxia is hypothesized to be the most common reason for hospital admission, our hope with the study was to show that the positive pressure nebulization would help improve the V/Q mismatch and atelectasis that caused the hypoxia in these patients. As a result of our study, an association between hospital admission rate with positive pressure nebulization or standard nebulization was not able to be determined due to a lack of statistical significance with our results. Our study was primarily limited by a small sample size and poor documentation of drug administration to be able to clearly distinguish between the two treatment groups. Further studies are indicated in order to show any benefit of positive pressure nebulization over standard nebulization in improving outcomes measured by admission rate, length of stay, and unscheduled returns to the emergency department.

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