Duration of Hospitalization in Association with Type of Inhalation Therapy Used in the Management of Children with Nonsevere, Acute Bronchiolitis

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Key Words
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Background: Acute bronchiolitis is one of the main respiratory emergencies in young children. Although supportive therapy is recommended, substantial inconsistency in the clinical usage of inhaled treatments has been reported. In the present study, we evaluated the association between different types of nebulized therapies in clinical practice and the length of stay (LOS) of young children hospitalized with nonsevere bronchiolitis.

Methods: Medical records of 195 patients with bronchiolitis, without evidence of pneumonia or congenital/chronic respiratory conditions, were stratified with respect to the type of inhalation therapy received: nebulized albuterol (Group 1, n = 53), nebulized albuterol with 3% saline (Group 2, n = 38), nebulized 3% saline alone (Group 3, n = 33), or no inhaled treatment (Group 4, n = 71). Duration of hospital stay was reported with respect to the type of inhalation therapy received after controlling for variability in patient age (months), oxygen saturation, respiratory score, and use of other treatments (antibiotics, oxygen supplementation, and/or corticosteroids). LOS is presented in terms of mean and 95% confidence interval (95% CI).

Results: The groups were similar except for differences in the mean level of oxygen saturation, respiratory score, and corticosteroid use. Children in Group 4 had the lowest mean respiratory score due to a lesser prevalence of wheezing and/or retractions than in other groups. The LOS for children in Groups 1 and 4 was shorter (43.2 hours, 95% CI 34.9–51.3, and 44.1 hours, 95% CI 37.3–51.0, respectively) than in Groups 2 and 3 (72 hours, 95% CI 62.1–81.6, and 65.1 hours, 95% CI 54.7–75.6, respectively) (p < 0.02). The mean LOS in each group did not change significantly after adjustment for covariants.

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1. Introduction

Acute bronchiolitis is a viral respiratory infection that occurs in children younger than 2 years, associated with the development of edema, mucus plugging, and obstruction of the lower airways. Although, in general, acute bronchiolitis is a self-limited condition, children with moderate-to-severe respiratory distress, deoxygenation, and dehydration require hospitalization for observation and supportive therapy. Acute bronchiolitis has been recognized as the main respiratory emergency leading to hospitalization of up to 3% of young children diagnosed with the condition. Of the total annual hospital charges in the USA, around 2 billion dollars are attributed to hospitalization of children with bronchiolitis. Pharmacological therapies for bronchiolitis with corticosteroids, antibacterials, antivirals, and/or bronchodilators are not recommended by the American Academy of Pediatrics for the routine management of hospitalized children. Although the evidence does not support routine administration of bronchodilators, their use in the clinical management of bronchiolitis is relatively frequent and varies widely between clinical settings. A number of studies have examined the effect of inhaled hypertonic saline (HS) on bronchiolitis outcomes and show an overall reduction in the length of stay (LOS) and good tolerability of inhaled HS treatments in children with mild-to-moderate bronchiolitis. However, others have reported no benefit or a negative impact of nebulized 3% saline on the clinical course of bronchiolitis, including respiratory function and/or LOS. Inconsistency in the medical literature and variability in the usage of inhaled therapy highlight the need for further evaluation of bronchiolitis outcomes in relation to management in the inpatient setting. In the present report, we evaluated the duration of hospitalization of young children with nonsevere bronchiolitis in association with the type of nebulized therapy used (albuterol, albuterol with 3% HS, 3% HS, or no inhaled treatment with bronchodilators and/or HS) in the inpatient setting, after accounting for variability in patients’ age, clinical presentation of disease, and inclusion of other medications in treatment.

2. Methods

We conducted a retrospective review of the medical records of children hospitalized with bronchiolitis between October 2009 and September 2012 at the Jersey Shore University Medical Center, Neptune, NJ, USA. We identified bronchiolitis cases from the hospital’s administrative database, using the International Classification of Diseases, Ninth Revision codes for bronchiolitis (466.11 and 466.19). This study is a secondary analysis of collected bronchiolitis cases to determine the relationship between LOS of young children hospitalized with bronchiolitis and types of nebulized medications included in their treatment. Children aged < 2 years, born at term gestation, without chronic conditions (lung disease, asthma, immunodeficiency, congenital heart disease, or cystic fibrosis), and without evidence of chest radiography-confirmed pneumonia and/or admission to the pediatric intensive care were eligible for inclusion in this analysis. Demographics (age and gender), medical history (history of eczema or wheezing, and family history of asthma), clinical data at admission (oxygen saturation, respiratory rate, wheezing, air exchange, and retractions), laboratory data (white blood cell count), and treatments administered (supplemental oxygen, corticosteroids, antibiotics, inhaled bronchodilator, and/or 3% HS) were extracted from the medical records of selected patients using a standardized collection tool that was approved by the Meridian Health Institutional Review Board of Jersey Shore University Medical Center in Neptune, NJ, USA.

Respiratory symptoms at admission (respiratory rate, wheezing, air exchange, and retractions) listed in the medical records were used to calculate and categorize the respiratory scores, as < 3 versus ≥ 3. Hypoxia at admission was defined as oxygen saturation (SpO2) of < 90% because oxygen supplementation is recommended for patients whose SpO2 is < 90%. LOS was defined as the difference in hours between admission and discharge. The time of discharge was identified by the attending pediatrician’s order in each of the bronchiolitis cases. We defined the study population as patients with nonsevere bronchiolitis, because patients were from the general pediatric ward and did not require continuous positive airway pressure and/or intubation during the course of disease.

2.1. Data presentation and statistical analysis

LOS for children hospitalized with bronchiolitis was analyzed with respect to the types of solutions used for nebulized therapy: 1.25 mg/3 mL (isotonic standard solution) albuterol every 4 hours prior to discharge (Group 1), 1.25 mg of albuterol with 4 mL of 3% HS every 4–6 hours prior to discharge (Group 2), 4 mL of 3% HS alone every 6–8 hours prior to discharge (Group 3), and no inhaled treatments (Group 4).

We compared demographic and clinical data of the groups using Chi-square and analysis of variance for categorical and continuous variables, respectively. The LOS for children included in each group is presented before and after correction for potential confounders.
after controlling for potentially clinically significant factors or those that were found to be significantly \((p < 0.05)\) associated with the outcome in unadjusted analyses using a general linear model. Data were analyzed statistically using STATISTICA 12 (StatSoft Inc., Tulsa, OK, USA) and are presented as proportion (%), mean \pm standard deviation, and 95% confidence interval (95% CI).

3. Results

Of the 232 patients identified via the administrative database, 195 met the inclusion criteria. Among them, 53 (27.2%), 38 (19.5%), 33 (16.9%), and 71 (36.4%) received nebulized treatments with albuterol solution alone (Group 1), albuterol solution with 3% HS (Group 2), 3% HS alone (Group 3), or no inhaled treatment (Group 4), respectively. Overall, inhaled nebulized treatments with 3% HS were used in the management of 36.4% of children (Groups 2 and 3) and albuterol in 46.7% (Groups 1 and 2). Differences were recorded between groups for the mean level of SpO2\%, respiratory score, and use of corticosteroids (Table 1). Children in Group 4 had the lowest mean respiratory score, and the number of children with respiratory scores \(\geq 3\) was higher in Groups 1 and 2 compared to that in Groups 3 and 4. As shown in Figure 1, wheezing and/or retractions were less likely to be recorded for patients in Group 4 as compared to patients in Groups 1–3. The LOS for children in Groups 1 and 4 was significantly shorter than that in Groups 2 and 3 (Figure 2). As shown in Figure 2, the mean LOS in each group did not change significantly after adjustment for age, SpO2\%, respiratory score, and use of oxygen, antibiotics, or corticosteroids. No adverse event association with inhaled therapy administration was recorded.

4. Discussion

This study evaluates the effect of differences in clinical practice with regard to the use of inhaled therapies on the duration of hospitalization of children with nonsevere bronchiolitis, at a single inpatient setting. More than one-third of patients received no inhalation therapy and an equivalent number received HS in nebulized solution with or without albuterol. Almost half of patients received nebulized albuterol alone or in combination with HS. The

### Table 1 Comparison of demographic and clinical variables with respect to treatment type for children hospitalized with bronchiolitis.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1* ((n = 53))</th>
<th>Group 2† ((n = 38))</th>
<th>Group 3‡ ((n = 33))</th>
<th>Group 4§ ((n = 71))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mo)</td>
<td>6.1 ± 5.3</td>
<td>5.0 ± 4.8</td>
<td>4.1 ± 3.9</td>
<td>4.6 ± 5.4</td>
<td>0.31</td>
</tr>
<tr>
<td>Age (\leq 12) (mo) (%)</td>
<td>88.7</td>
<td>89.5</td>
<td>93.9</td>
<td>91.5</td>
<td>0.09</td>
</tr>
<tr>
<td>Feeding (any breast milk) (%)</td>
<td>24.4</td>
<td>30.3</td>
<td>25.8</td>
<td>40.6</td>
<td>0.13</td>
</tr>
<tr>
<td>Gender: male (%)</td>
<td>56.6</td>
<td>71.0</td>
<td>63.6</td>
<td>46.5</td>
<td>0.08</td>
</tr>
<tr>
<td>History of wheezing &amp;/or eczema (%)</td>
<td>13.2</td>
<td>10.5</td>
<td>6.1</td>
<td>5.6</td>
<td>0.45</td>
</tr>
<tr>
<td>Family history of asthma (%)</td>
<td>32.1</td>
<td>35.1</td>
<td>40.6</td>
<td>37.1</td>
<td>0.97</td>
</tr>
<tr>
<td>WBC (&gt; 15,000) mm(^3) (%)</td>
<td>17.8 (8/45)</td>
<td>13.9 (5/36)</td>
<td>10.7 (3/28)</td>
<td>26.3 (15/57)</td>
<td>0.26</td>
</tr>
<tr>
<td>SpO2%</td>
<td>96.3 ± 3.1</td>
<td>96.6 ± 3.3</td>
<td>97.1 ± 2.8</td>
<td>97.9 ± 2.2</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>SpO2 ≤ 90% (%)</td>
<td>3.8</td>
<td>5.3</td>
<td>6.1</td>
<td>1.4</td>
<td>0.56</td>
</tr>
<tr>
<td>Respiratory score</td>
<td>1.3 ± 0.9</td>
<td>1.4 ± 1.1</td>
<td>1.3 ± 1.0</td>
<td>0.69 ± 0.80</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Respiratory score (\geq 3) (%)</td>
<td>42.1</td>
<td>35.1</td>
<td>14.3</td>
<td>5.4</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Corticosteroid use (%)</td>
<td>11.5</td>
<td>7.9</td>
<td>0</td>
<td>0</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Antibiotics use (%)</td>
<td>30.2</td>
<td>23.7</td>
<td>36.4</td>
<td>23.9</td>
<td>0.53</td>
</tr>
<tr>
<td>(O_2) supplementation (%)</td>
<td>26.4</td>
<td>36.8</td>
<td>27.3</td>
<td>22.5</td>
<td>0.46</td>
</tr>
</tbody>
</table>

\(O_2 = \) oxygen; SpO2 = pulse oximetry level; WBC = white blood cell count.

* Group 1 received nebulized albuterol only.
† Group 2 received nebulized albuterol + 3% saline.
‡ Group 3 received nebulized 3% saline only.
§ Group 4 received no inhaled treatment.
¶ Included patients ≤ 12 months old.
Inclusion of 3% HS in inhaled therapy and no additional bronchodilators, all call into question the beneficial effects of nebulized albuterol without 3% HS, regardless of age, respiratory score, use of oxygen, antibiotics, and corticosteroids. Group 1 received nebulized albuterol only. Group 2 received nebulized albuterol + 3% saline. Group 3 received nebulized 3% saline only. Group 4 received no inhaled treatment. CI = confidence interval; LOS = length of stay.

LOS for patients who did not receive any inhaled therapy was comparable to that of patients who were treated with nebulized albuterol without 3% HS, regardless of age, respiratory symptoms, and use other treatments. The obtained results are similar to those of reports from small and heterogeneous placebo (inhaled normal saline) controlled trials that show no beneficial effect of routine use of bronchodilators on the LOS of children with bronchiolitis. Inclusion of inhaled 3% HS in the treatment of our patients was associated with prolongation of their hospitalization, independent of other covariants. Our findings are contrary to those of other reports that show a 1-day mean reduction in the duration of hospitalization for children with bronchiolitis using inhaled HS or no effect of inhaled HS on the LOS. Nevertheless, variability in dosage regimens and cointerventions, as well as no short-term improvement in clinical scores with inclusion of 3% HS in inhaled therapy and no additional benefit of adding 3% HS to nebulized solution with bronchodilators, all call into question the beneficial effects of 3% HS. A revised American Academy of Pediatrics clinical practice guideline published in 2014 identified administration of nebulized HS to infants and children hospitalized for bronchiolitis as a weak recommendation due to inconsistent findings.

Although our study is observational in nature, the results were controlled for the important covariants that may, along with the type of nebulized therapy administered, influence the duration of hospitalization in children with bronchiolitis. In addition to age and respiratory score, we included oxygen level and oxygen supplementation in the model because of the reported associations of the need for oxygen supplementation and lower pulse oximeter readings with a longer LOS. We also controlled for the use of antibiotics in the regression analysis because longer hospitalization of children with bronchiolitis who were treated with antibiotics has been reported, although a recently published Cochrane review showed no effect of use of antibacterial therapy on the LOS of children younger than 2 years who were hospitalized with bronchiolitis.

We acknowledge several limitations of the present report that may affect the conclusions. Although the retrospective design increases the risk for bias in data collection and the effect of confounding variables, the following strategies were used to decrease the risk of bias and maintain internal validity: (1) standardization of the data collection tool; (2) precise measurement of LOS (in hours); (3) exclusion of bronchiolitis cases with evidence of pneumonia; and (4) control of important covariants for their possible association with the duration of hospitalization. Moreover, the power analysis showed that the sample size of 195 patients used in this study is sufficient to detect a 30% difference in the mean LOS between groups stratified by the type of nebulized therapy administered with a power of 87% and $\alpha < 0.05$. We admit that the weakness of using data from a single inpatient setting is uncertain generalizability of results to other practices. However, our investigation is based on the analysis of an age- and disease-specific population of patients with bronchiolitis, and additional analysis of 99 randomly selected cases from the 195 cases included in the database showed the same association between the LOS and type of nebulized therapy used for patients’ management: Group 1 ($n = 28$, 40.1, 95% CI 29.3–50.9 hours), Group 2 ($n = 18$, 69.6, 95% CI 48.6–90.5 hours), Group 3 ($n = 20$, 68.3, 95% CI 47.9–88.7 hours), and Group 4 ($n = 33$, 41.2, 95% CI 33.7–48.8 hours; $p < 0.0001$). Despite that, similar evaluation of nebulized therapies used in the routine clinical management of bronchiolitis may be needed to verify that the obtained results are reproducible in different settings. The role of demographic and clinical characteristics in addition to treatments administered should be assessed when determining the duration of hospitalization of children with bronchiolitis.

In conclusion, prolonged hospitalization of children younger than 2 years with acute, nonsevere bronchiolitis is associated with administration of nebulized 3% saline, independent of age, clinical presentation of disease, or inclusion of other treatments in their management.

Conflicts of interest

All authors declare no conflicts of interest related to this research study.

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