Undiluted Albuterol Aerosols in the Pediatric Emergency Department

David J. Gutglass, MD*; Louis Hampers, MD, MBA*; Genie Roosevelt, MD, MPH*; Doreen Teoh, MD*; Sai R. Nimmagadda, MD‡; and Steven E. Krug, MD*

ABSTRACT. Objective. To evaluate the efficacy and efficiency of a short treatment method of administering albuterol aerosols.

Methods. Fifty children 6 to 18 years of age with severe acute asthma (peak flow rates <60% of predicted) were enrolled in a single-blind, controlled trial in an urban pediatric emergency department. Patients were randomized to receive either the study short treatment (3.5 mL of undiluted albuterol nebulized for 20 inhalations) or the control treatment (albuterol diluted [5 mL] and nebulized in normal saline [3 mL]) every 20 minutes for a total of 3 treatments. Peak flow and spirometric measurements were performed before and after each treatment.

Results. There were 25 patients in the study group and 25 in the control group. There were no demographic differences between groups; both had comparable pulmonary function at presentation. The mean forced expiratory volume in 1 second percent predicted improvement between 0 and 60 minutes was 18.8% in the study group and 14.5% in the control group. The total time of treatment delivery for the study group was 6.4 minutes versus 32.7 minutes for the control group.

Conclusion. Undiluted albuterol short treatments seem to be as effective as standard diluted albuterol in severe asthma exacerbations, while offering the ease and efficiency of shorter treatment administration time. Pediatrics 2000;105(5). URL: http://www.pediatrics.org/cgi/content/full/105/5/e67; peak flow, forced expiratory volume in 1 second, spirometry, clinical asthma score, cost analysis.

ABBREVIATIONS. ED, emergency department; PEFR, peak expiratory flow rate; PRED, predicted; FEV1, forced expiratory volume in 1 second; ANOVA, analysis of variance; SD, standard deviation.

A cute asthma exacerbations are responsible for a large percentage of children who seek care in the emergency department (ED). The total societal cost of asthma has been estimated at $6.4 billion a year for the United States alone.1 According to the current asthma guidelines published by the National Institute for Health, β2-agonists are the standard first-line therapy in the acute setting.2 Although this class of pharmacotherapy has been studied extensively, practitioners have come to no consensus regarding the optimal β2-agonist concentration or the ideal method of delivery. A review of the literature suggests that the method of β-agonist delivery and its concentration are institution-specific.3

Although the highest dose of albuterol that can be used safely is not known, investigators have used higher concentrations than those recommended on the package insert. Early studies of asthma in children used .05 mg/kg of albuterol as a standard dose. Schub et al4 showed that a dose of .15 mg/kg resulted in marked improvement in pulmonary function without significant side effects. Subsequent studies have demonstrated the safety of continuous nebulized albuterol at doses of 3.4 mg/kg per hour; patients have been shown to tolerate up to 20 mg of albuterol per treatment without significant side effects.5-6 Given the improved efficacy and efficiency of higher doses, Durrani et al7 introduced a new technique for the delivery of nebulized albuterol. A 5-breath method of undiluted albuterol inhalation was used to deliver a higher concentration of medication in a shorter time period. We designed a randomized, single-blind, prospective study to assess the efficacy and efficiency of undiluted, nebulized albuterol and to compare it to standard diluted therapy in children with a severe asthma exacerbation. Our primary outcome variables were the change in peak expiratory flow rate predicted (PEFRPRED) and forced expiratory volume in 1 second predicted (FEV1PRED) over time between the control and study groups.

METHODS

A convenience sample of 50 patients with an acute asthma exacerbation who presented to the Children’s Memorial Hospital ED from March 1996 to April 1997 were enrolled. Patients were eligible for the study if they were between 6 and 18 years of age, were able to perform peak flow and spirometric maneuvers, and their peak flow measured <60% of predicted for age and height. Currently, published asthma guidelines suggest that a peak flow of <50% predicted is indicative of severe asthma.2 Aztec peak flow meters (Center Laboratory Division of EM Industries Inc, Port Washington, NY) were used for all patients and predicted values were derived from height and weight nomograms included in the package insert. To determine eligibility, the best of 3 efforts was recorded. Exclusion criteria included wheezing for the first time, history of congenital heart disease or other primary pulmonary disorder, and the need for emergent intubation. This study was approved by the Children’s Memorial Institutional Review Board. Written informed consent was obtained from the parents before patient enrollment. Assent was obtained for children >12 years of age.

The investigator was on call 24 hours a day. When the nurses at triage recognized a possible candidate for the study, the investigator was paged to the ED. The investigator was given 15 minutes to be at the patient’s bedside before standard therapy was initiated. This was a convenience sample because some patients were...
missed because either triage nurses failed to call the investigator for appropriate study subjects or the primary investigator was unable to respond within 15 minutes.

Children were randomly assigned to receive either the control treatment of 3 mL (2.5 mg) of undiluted albuterol in 3 mL of normal saline nebulized completely or the study short treatment of 3.5 mL (17.5 mg) of undiluted albuterol for 20 breaths every 20 minutes for a total of 3 treatments. We increased the treatment duration to 20 breaths because the 5-breath method was used on a younger population of children. Nebulization was performed with the Pari Respiratory Less Components Disposable device (Pari Respiratory, San Jose, CA) disposable nebulizer with tight-fitting oxygen mask with a flow rate of 6 L/minute. The randomization was performed in the hospital pharmacy in blocks of 10. The pharmacy prepared the control or study drug and placed it in a sealed envelope in a locked closet located in the ED. After enrollment by the investigator, the ED nurse opened the sealed envelope while in the patient room revealing the treatment plan. The investigator was not present during this time and during treatment administration. The total time of treatment delivery, which included equipment setup, was recorded by the ED nurse. The total treatment time for the control group included all 3 treatments from setup to finish and for the study group all 60 breaths. All patients were placed on a cardio-respiratory monitor and pulse oximeter for the entire study period. Blood pressure readings were obtained every 20 minutes. Oxygen was given to patients with oxygen saturations <93% when breathing room air. All patients received 2 mg/kg of prednisolone or prednisone after the first treatment was completed with a maximum of 60 mg.

All patients were assessed before and after each treatment in 20-minute intervals by a sole investigator (D.J.G.), who was unaware of treatment allocation. This clinical assessment included recording complete vital signs, assigning a modified Wood-Downes-Lecks asthma score, measuring peak flow, and taking spirometry measurements. We used a Multi-Spiro 5x Platinum program (Multi-Spiro, San Clemente, CA). Calibration was performed before each trial using Knudson/IMTS normals. At the end of the third treatment, the study registered nurse placed the data sheet, which included information about the treatment allocation and treatment time delivery, into a sealed envelope before delivering it to the investigator. The decision to hospitalize the patient, as well as all other treatment decisions after the study, were made by the ED attending, who was unaware of treatment allocation.

The primary analysis was the repeated-measures analysis of variance between the groups in changes in the PEFRPRED, FEV1PRED, and heart rate over the 60-minute study period. The required number of subjects was based on previous asthma trials. Continuous variables were analyzed with a Student’s t-test. The Wood-Downes-Lecks score differences at baseline and at 60 minutes were compared using Mann-Whitney U tests. Categorical data were analyzed by χ² tests.

RESULTS

Fifty patients were enrolled and completed the study. Twenty-five patients were in the study group and 25 patients in the control group. There were no differences between the groups in age or race. The study group had a higher percentage of males (P < .02; Table 1). The groups did not differ in duration of symptoms, presence of fever, or baseline PEFR and FEV₁ (Table 2). Use of asthma medications and health care facilities were also similar for both groups (Table 2).

### TABLE 1. Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in y (mean ± SD)</td>
<td>10.8 ± 3.3</td>
<td>10.2 ± 2.8</td>
</tr>
<tr>
<td>Male %*</td>
<td>19 (76%)</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>White</td>
<td>1 (4%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Black</td>
<td>14 (56%)</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>9 (36%)</td>
<td>10 (40%)</td>
</tr>
</tbody>
</table>

* P < .02.

### TABLE 2. Clinical Characteristics at Presentation

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>11 (44%)</td>
<td>12 (48%)</td>
</tr>
<tr>
<td>Upper respiratory infection symptoms</td>
<td>20 (49%)</td>
<td>21 (51%)</td>
</tr>
<tr>
<td>PEFRPRED ± SD</td>
<td>40 ± 9</td>
<td>36 ± 11</td>
</tr>
<tr>
<td>FEV₁PRED ± SD</td>
<td>31 ± 11</td>
<td>33 ± 12</td>
</tr>
<tr>
<td>β-agonist within 1 h</td>
<td>12 (48%)</td>
<td>8 (32%)</td>
</tr>
<tr>
<td>Sees allergist</td>
<td>6 (24%)</td>
<td>6 (24%)</td>
</tr>
<tr>
<td>&gt;2 ED visits last 12 mo</td>
<td>11 (44%)</td>
<td>13 (52%)</td>
</tr>
<tr>
<td>Hospitalized in last 12 mo</td>
<td>11 (44%)</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>Taking prednisone</td>
<td>4 (16%)</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Sa₀₂ on RA at time 0 (mean ± SD)</td>
<td>95 ± 2</td>
<td>95 ± 4</td>
</tr>
<tr>
<td>Sa₀₂ on RA at time 60 (mean ± SD)</td>
<td>95 ± 3</td>
<td>96 ± 3</td>
</tr>
<tr>
<td>WD score time 0 (mean ± SD)</td>
<td>4.0 ± 1.1</td>
<td>3.8 ± .93</td>
</tr>
<tr>
<td>WD score time 60 (mean ± SD)</td>
<td>1.8 ± 1.3</td>
<td>1.5 ± 1.2</td>
</tr>
</tbody>
</table>

RA indicates room air; WD, Wood-Downes.

The primary analysis was the repeated-measures analysis of variance. The mean increase in PEFRPRED improvement between time 0 and 60 minutes was 23.7% in the study group and 22.5% in the control group (Table 3). There was a significant time effect (P < .001); that is, both groups showed a statistically significant improvement in PEFRPRED over the 60-minute study. However, repeated-measures analysis of variance (ANOVA) showed no statistically significant difference between the study and control groups (P = .46; Fig 1). The mean increase in FEV₁PRED improvement between time 0 and 60 minutes was 18.8% in the study group and 14.5% in the control group (repeated-measures ANOVA, P = .66). There was a significant time effect (P < .001; Fig 2). The average clinical score improvement between 0 and 60 minutes was 2.3 in the study group and 2.2 in the control group (P = .65).

Although the total treatment times were fixed in both groups to maintain physician blinding, the differences between groups in actual duration of drug administration was statistically significant (P < .001; Table 3). On average, a total of 32.7 minutes of nursing time were spent administering albuterol to the control group, versus 6.4 minutes in the study group.

There were no adverse side effects in patients of either group. The mean increase in heart rate did not differ between the 2 groups. There was a trend toward a higher admission rate in the control group but this was not statistically significant (P = .08; Table 3).

### DISCUSSION

Our study demonstrates that short treatments of albuterol are a safe and effective means of treating children in the ED with severe asthma. During the 60-minute study, we observed a comparable improvement in PEFRPRED and FEV₁PRED for both treatment groups. This study has taken a novel approach to improve the efficiency and ease of albuterol administration in the ED. These short treatments provide a substantial advantage for respiratory therapists, nurses, physicians, and most importantly, for our patients. The method of delivery is quick, easy, and well-tolerated.

A review of the literature suggests a progression of albuterol dosing. Schuh et al showed that increasing the albuterol dose from .05 mg/kg per treatment to...
.15 mg/kg resulted in improved pulmonary function without significant side effects. The current minimal dose of albuterol for treatments of acute exacerbations of asthma in childhood is .15 mg/kg. In recent years, several studies have advocated even higher doses of albuterol with continuous nebulization in the intensive care setting. These doses range as high as 3.4 mg/kg ± 2.2 per hour. Although we did not measure the quantity of albuterol delivered to the short treatment group, the maximum possible dose over the course of 3 treatments was .42 mg/kg ± .19. Our higher dosing is consistent with the National Institutes of Health recommendations of .15 mg/kg per treatment every 20 minutes for the first hour. One possible explanation for the advantage of higher dosing may be better lung penetration because it is estimated only ~10% reaches the lung. This may have explained the trend toward decreased hospitalization in the study group. However, we did not perform any formal measurements of albuterol delivery in this study and we did not have the necessary power to detect a difference in admission rate. Perhaps an area of further research would be to examine more patients with this method and compare admission rates in a blinded fashion.

There are several ways in which short treatments may increase the efficiency of ED asthma care. Our study demonstrated a 26-minute decrease in nursing time spent administering treatments. Although close monitoring of these patients is still required, this reduction may increase the flexibility of staff in a busy ED setting. Our methodology prevented us from examining differences in ED lengths of stay. However, it is conceivable that shorter treatments would also result in shorter ED visit times. Additional cost savings are suggested by a decreased ED admission rate in study group. The net effect of short treatment albuterol on ED efficiency remains to be quantified, but it clearly shows promise compared with standard therapy in the ED. Durrani et al suggested that this method might be appropriate for younger children in whom compliance with the traditional nebulization over 15 to 20 minutes can be difficult. We believe that future studies should focus on this younger age group.

Our study has some limitations. We used a convenience sample of patients who may not be representative of the population of children who seek care in the ED for severe acute asthma. However, because we included only those patients whose PEFRPRED was <60%, we ensured that all patients were of similar high acuity. We chose a sample size similar to that of other asthma treatment trials. Unfortunately, our sample size was small; thus, our inability to detect a difference between the 2 groups may be a result of a type II error. We did not evaluate differences in lengths of time in the ED. The use of undiluted albuterol may have resulted in shorter ED visit times. This may translate into additional cost savings. A formal analysis of cost was not performed in this study but may represent an area of future investigation.

CONCLUSION

Undiluted albuterol short treatments are as effective as standard diluted albuterol for children with severe acute asthma treated in the ED. This method offers easy administration, efficient delivery, and may provide cost savings.
REFERENCES


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