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Pediatrics 2005;116:1127
DOI: 10.1542/peds.2004-2136

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Helium/Oxygen-Driven Albuterol Nebulization in the Treatment of Children With Moderate to Severe Asthma Exacerbations: A Randomized, Controlled Trial

In K. Kim, MD*; Erin Phrampus, MD, MPH*; Shekhar Venkataraman, MD†; Raymond Pitetti, MD, MPH*; Al Saville, RRT‡; Timothy Corcoran, PhD§; Ed Gracely, PhD||; Nicole Funt, MPAS, PA-C*; and Ann Thompson, MD‡

ABSTRACT. Background. Helium and oxygen mixtures (heliox) increase both pulmonary aerosol delivery and gas delivery relative to oxygen. We aimed to compare the effectiveness of a 70%/30% helium/oxygen (heliox)–driven continuous aerosol delivery versus 100% oxygen–driven delivery in the treatment of asthmatic children with moderate to severe exacerbations.

Methods. We enrolled 30 children aged 2 to 18 years who presented to an urban, pediatric emergency department (ED) with moderate to severe asthma as defined by a pulmonary index (PI) score of ≥8. PI scores can range from 0 to 15. In this randomized, controlled, single-blind trial conducted in a convenience sample of children, all patients in the trial received an initial nebulized albuterol (5 mg) treatment driven by 100% oxygen and a dose of oral prednisone or prednisolone. Subsequently, patients were randomly assigned to receive continuously nebulized albuterol (15 mg/hour) delivered by either heliox or oxygen using a nonrebreathing face mask. The primary outcome measure was degree of improvement as assessed in blinded video-recorded PI scores over 240 minutes (at 30-minute intervals for the first 3 hours) or until ED discharge (if <240 minutes).

Results. The mean change in PI score from baseline to 240 minutes or ED discharge was 6.67 for the heliox group compared with 3.33 for the oxygen group. Eleven (73%) patients in the heliox group were discharged from the hospital in <12 hours compared with 5 (33%) patients in the conventional group.

Conclusion. Continuously nebulized albuterol delivered by heliox was associated with a greater degree of clinical improvement compared with that delivered by oxygen among children with moderate to severe asthma exacerbations. Pediatrics 2005;116:1127–1133; asthma, emergency department, heliox, pediatric.

ABBREVIATIONS. ED, emergency department; heliox, helium/oxygen mixture; PI, pulmonary index.

The use of β2-agonist agents in the emergency department (ED) management of acute asthma has clearly been established. Studies have demonstrated more favorable responses in patients treated with continuous nebulization compared with intermittent administration, suggesting that optimizing drug delivery is an important therapeutic consideration.1–4 The use of a helium/oxygen (heliox) mixture to facilitate aerosol delivery may further optimize β2-agonist therapy for patients with asthma exacerbations. Heliox may optimize β2-agonist delivery because of its lower gas density, leading to decreased flow resistance and increased aerosol penetration into the lungs.5,6

Rodrigo et al7 published a Cochrane systematic review of heliox for asthma therapy and concluded that heliox had no effect on pulmonary function. It is important to note that this review focused on the use of heliox alone and primarily in adults, not on the use of heliox as a driving gas for nebulizing β2-agonist therapy. Also, this review included only a single pediatric study that did not use heliox as a driving gas for nebulizing β2-agonist therapy and for a brief duration of 15 minutes. In summary, these authors conclude that many questions regarding the treatment of acute asthma with heliox remain unanswered. They suggested that additional studies needed to be conducted involving the pediatric population.

The objective of this study was to evaluate the efficacy of heliox versus oxygen in driving continuous albuterol nebulization in children with moderate to severe asthma. We hypothesized that children with moderate to severe exacerbations of asthma treated with nebulized albuterol driven by heliox would have more clinical improvement, as assessed by an asthma-severity score, than those who received nebulized albuterol driven with oxygen.

METHODS

Participants

This study was conducted between October 2001 and May 2002 in the ED of an urban, tertiary care children’s hospital. The insti-
tutional review board approved the study. The study was re-
vieved and approved by the US Food and Drug Administra-
tion (FDA) and assigned FDA-IND 61783. Informed consent was ob-
tained from the parent or guardian of each child. Written assent
was obtained from all patients who were ≥6 years old.

Entry criteria for study subjects included (1) age 2 to 18 years,
(2) pulmonary index (PI) score of ≥8 (Table 1),8–10 (3) availability
of a study investigator (convenience sample), (4) written assent
2 years were not enrolled to avoid enrolling patients with bron-
costeroids within the preceding 72 hours. Children younger than
nonrebreather face mask, and the use of oral or parenteral corti-
ony syncytial virus enzyme-linked immunosorbent assay, lobar
quences (70%:30% helium/oxygen) were initiated with each patient
in the study.

Study Protocol

The clinical scoring system used was a PI score8 based on respira-
tory rate, wheezing, accessory respiratory muscle use, inspi-
atory/expiratory ratio, and pulse oximetry. The maximum
possible score was 15, and a PI score of ≥8 defined moderate to
severe disease. The PI score has been shown to correlate signifi-
cantly with pulmonary-function tests and hospitalization rates in
children older than 6 years treated for acute asthma.9 In addition,
the PI has been used to assess younger children.11 Subsequently,
the PI has been modified to better identify and assess moderately
ill asthmatic children.8,10

On presentation in the ED, all potential enrollees were treated
with 5 mg of inhaled albuterol via face mask from a HEART
nebulizer (Westmed Inc., Englewood, CO) driven by 100% oxygen
at a flow of 10 L/minute. A timeline of methods is illustrated in
Fig 1. Although the patient was being treated with this initial
albuterol nebulization, a research assistant identified the patient as
eligible for enrollment and then notified the investigator who was
on call for the study.

The investigator examined the patient and assigned a PI score.
Patients who achieved a clinical score of ≥8 and met all eligibility
criteria were invited to participate in the study. During the com-
pletion of the first 20 minutes of nebulized albuterol treatment, all
patients received oral steroids (prednisone or prednisolone, 2
mg/kg; maximum dose: 60 mg). If they did not tolerate oral
steroids, as defined by vomiting within 30 minutes, intravenous
access was established and patients were given an intravenous
dose (2 mg/kg) of methylprednisolone to a maximum dose of 125
mg. After completion of 20 minutes of nebulized albuterol, pa-
tients were randomly assigned to either the heliox or oxygen
group. ED discharge was determined by an unblinded pediatric
emergency medicine attending physician who did not participate
in the study.

Randomization was predetermined by using a random-number
generator and occurred in blocks of 10. Assignments were kept in
sealed envelopes. Fifteen patients were randomly assigned to the
heliox group, and 15 patients were randomly assigned to the
oxygen group.

Heliox or oxygen mixtures were administered from the nebu-
lizer via a nonrebreathing face mask at room temperature (20°C).
Heliox was administered via a CGA (compressed gas association)
280 regulator driven by a standardized pressure of 50 lb per
square inch gauge. To ensure a standard albuterol delivery rate of
15 mg/hour, oxygen flows of 10 L/minute and heliox flows of 16
L/minute were used. The respiratory therapists were unblinded
to the study as they monitored the mixing of gases at the blender.
Thereafter, patients in each arm of the study received 15 mg/hour
of albuterol for 1 hour followed by 500 μg of ipratropium bromide
(Atrovent) over 5 minutes. At the end of the first hour of contin-
uous albuterol therapy and after 1 dose of ipratropium bromide,
patients who had a PI score of ≥3 as assessed by the unblinded
recruiting investigator received a second hour of continuous al-
buterol (15 mg/hour) followed by a second dose of 500 μg of
ipratropium bromide. At the end of the second hour of continuous
albuterol, patients who had a PI score of ≥3 as assessed by the
unblinded recruiting investigator received a third hour of contin-
uous albuterol (15 mg/hour).

Percentages of inspired oxygen were measured at the level of
the patient’s face mask and titrated to maintain patient oxygen
saturation of ≥93% as measured by pulse oximetry. Heliox mix-
tures (70%:30% helium/oxygen) were initiated with each patient
in the heliox group. If necessary, patients in the heliox group were
given a maximum titration of 50%:50% helium/oxygen to main-
tain patient oxygen saturation of ≥93%. Those patients requiring
>50% oxygen were designated as treatment failures, and they
were taken off the heliox mixtures and treated with 100% oxygen
therapy.

Time 0 was the time that the study drug (heliox or oxygen) was
given. Clinical assessments were performed at the initiation of
heliox or oxygen and then at 30, 60, 90, 125, 150, 180, and 240
minutes after time 0. Clinical assessments were completed by
using a recordable electronic stethoscope (Simulscope II; Cardion-
ics, Webster, TX) and a Panasonic (Secaucus, NJ) 120 VHS-C video
camcorder. A standardized recorded auscultatory examination cov-
ering 4 positions on the anterior and posterior chest (8 total) for 2
breaths per position (16 breaths total) were completed by the
recruiting investigator to determine the presence and absence of
inspiratory and expiratory wheezing. In addition, this examina-
tion served to determine respiratory rate and inspiratory/expira-
tory ratio as assessed by the blinded investigator using recorded
data. Patients were asked to raise their shirt to the lower costal
margin and to lower their shirt collar inferior to the clavicle to
determine accessory muscle use. Additionally, oxygen saturation
was recorded after 2 minutes on room air. A blinded scorer, an
investigator who did not recruit or care for the patient, later scored
the videotape and recorded a PI score. Data shown in Fig 2 are the
video-recorded PI scores recorded by this blinded investigator. A
single scorer was used to minimize interobserver variability.

The advantage of this video-recorded PI was that it served to
maintain blinding of our study. Because of the voice-pitch changes
associated with heliox mixtures, blinding by the recruiting inves-
tigator could easily be lost. Patients were asked not to speak
during the recording periods of the PI, each period lasting ~2
minutes.

Before the initiation of the study, a standardized video-re-
corded PI examination was piloted and validated for accuracy and
reproducibility in 8 patients by the principal investigator. During
the pilot trial, the video-recorded PI was compared with a stan-
dard PI. The standard PI was defined as the PI scored by the
principal investigator. Spearman correlations comparing the vide-
orecorded PI to the standard PI ranged in intraclass variables
from 0.958 to 1.0. Mean differences between investigators never
exceeded 1 point and did not substantially affect the estimated
correlations.

| TABLE 1. PI: Clinical Asthma Evaluation Score<sup>8–10</sup> |
|-----------------|--------|--------|--------|--------|
| Variables       | 0      | 1      | 2      | 3      |
| Respiratory rate, respirations per min* | ≤30    | 31–45  | 46–60  | >60    |
| Wheezing†       | None   | End expiration | Entire expiration | Inspiratory and expiration without stethoscope |
| Inspiratory/expiratory ratio | 2:1    | 1:1    | 1:2    | 1:3    |
| Accessory muscle used | None   | +      | ++     | +++    |
| Oxygen saturation | 99–100 | 96–98  | 93–95  | <93    |

* Indicates mild; ++, moderate; ++++, severe.
† If no wheezing due to minimal air entry, score 3.
The ordering of chest radiographs was made at the discretion of the ED attending physician who was managing the patient. All enrolled patients received 24-hour and 7-day follow-up after discharge. Follow-up entailed the use of a pager, cell phone, or best contact telephone number and followed a structured questionnaire.12

### Statistical Analyses

Before the study began, a clinically significant improvement in the PI was defined as an increase of ≥2 units over time, as was a difference of ≥2 units between groups at any point in time. To calculate sample size, 2 units were considered to be the minimum relevant difference.9,10 Based on the SD for a change in PI score found in previous studies of asthmatic children with a similar degree of illness (pooled SD: 1.97) and setting α at .05, 30 children (15 in each group) were needed for a study power of 80%.9,10

The primary outcome measure was the degree of improvement as assessed by PI scores over 240 minutes (at 30-minute intervals for the first 3 hours) or until ED discharge (if <240 minutes); 240 minutes has been shown to be an optimal time frame to examine

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### Table: Interventions

<table>
<thead>
<tr>
<th>Time</th>
<th>-Eligibility criteria assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Consent obtained</td>
<td>-Albuterol 15 mg/h for 60 min</td>
</tr>
<tr>
<td>-Randomly assigned to receive 100% O₂ or 7%–50% helium/oxygen</td>
<td>Reassess, if PI ≥ 3 continue albuterol 7.5 mg/h</td>
</tr>
<tr>
<td>-Albuterol 15 mg/h for 60 min</td>
<td>Disposition (admit or discharge)</td>
</tr>
</tbody>
</table>

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### Figure 1. Time line in emergency department.

![Fig 1. Time line in emergency department.](image1)

### Figure 2. Mean PI scores versus time.

![Fig 2. Mean PI scores versus time.](image2)

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**Table:**

<table>
<thead>
<tr>
<th>Mean PI, oxygen (±SD)</th>
<th>Time 0</th>
<th>30 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
<th>150 min</th>
<th>180 min</th>
<th>240 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.7 ± 1.5</td>
<td>9.1 ± 1.5</td>
<td>8.8 ± 1.6</td>
<td>7.9 ± 1.3</td>
<td>7.9 ± 2.3</td>
<td>7.3 ± 2.2</td>
<td>7.5 ± 2.3</td>
<td>6.5 ± 2.2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean PI, heliox (±SD)</th>
<th>Time 0</th>
<th>30 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
<th>150 min</th>
<th>180 min</th>
<th>240 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.7 ± 1.5</td>
<td>9.4 ± 1.7</td>
<td>8.3 ± 1.7</td>
<td>7.0 ± 1.6</td>
<td>6.1 ± 2.1</td>
<td>4.9 ± 2.3</td>
<td>4.7 ± 2.0</td>
<td>4.2 ± 2.4</td>
<td></td>
</tr>
</tbody>
</table>

| ΔPI oxygen–heliox     | -1.0   | -0.3   | 0.5    | 0.9    | 1.8     | 2.4     | 2.8     | 2.3     |

| P values              | 0.096  | 0.655  | 0.449  | 0.313  | 0.029   | 0.006   | 0.001   | 0.008   |

95% Confidence intervals:

- Oxygen: -2.049 to 0.18
- Heliox: -1.48 to 0.64
- ΔPI oxygen–heliox: -0.78 to 1.71
- ΔPI oxygen–heliox: 0.007 to 2.69
- ΔPI oxygen–heliox: 0.21 to 3.53
- ΔPI oxygen–heliox: 0.39 to 3.57
- ΔPI oxygen–heliox: 1.29 to 4.45
- ΔPI oxygen–heliox: 0.78 to 4.58

**Fig 2. Mean PI scores versus time.**

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**Statistical Analyses**

Before the study began, a clinically significant improvement in the PI was defined as an increase of ≥2 units over time, as was a
the effects of both aerosolized medications and systemic corticosteroids for acute asthma in the ED.\textsuperscript{9}

Simple comparisons between groups or categorical variables were made with the $\chi^2$ or Fisher's exact test. The Mann-Whitney $U$ test was used to compare the mean changes in PI over time. Two-way analysis of variance was performed for both groups. Normality of the PI and change in PI were confirmed by using the skewness measure provided by SPSS 8 (SPSS Inc, Chicago, IL) software. Other assumptions of the analysis of variance were tested by SPSS and then corrected as needed.

RESULTS

A total of 75 patients in a convenience sample were screened for study enrollment (Fig 3). Thirty-five children met the eligibility criteria. Of these 35 children, 4 patients' parents refused to participate and 1 child in the heliox group (2.05 years old) met exclusion criteria because he did not tolerate the face mask after 5 minutes, leaving a total of 30 patients. Fifteen children completed treatment with heliox-driven albuterol nebulization, and 15 completed treatment with oxygen-driven albuterol nebulization. There were no treatment failures in either group.

No significant differences at study entry were found between the treatment groups with respect to gender, race, or age (Table 2). The duration of wheezing and recent use of asthma medications was also similar between groups (Table 2). Children in each group had equivalent severity of illness at initial presentation as reflected by a comparison of mean PI scores ($P = .10$) and initial pulse oximetry ($P = .10$).

Mean video-recorded PI scores assessed by the
blinded investigator for each assessment time in the first 4 hours are shown in Fig 2. This video-recorded approach ensured that the scorer did not lose blindness when reviewing the recorded videotape to assign a PI score. The mean change in PI score from baseline to 240 minutes was 6.67 for the heliox group compared with 3.33 for the oxygen group ($P < .001$). At 125 minutes, the heliox group showed a clinically significant absolute mean PI improvement compared with the oxygen group ($P < .05$). A clinically significant difference of absolute mean PI scores ($P < .01$) was sustained at 150, 180, and 240 minutes.

In addition, 2-way analysis of variance found evidence for a benefit from heliox-driven albuterol. Group main effect (a comparison of overall means, $P < .05$) as well as the interaction between time and group (a comparison of the pattern of changes over time between groups, $P < .001$) was significant.

At baseline, the heliox group’s average PI score was higher by 1 point than the oxygen group’s average PI score (10.7 vs 9.7). Our analysis included this baseline difference. By 240 minutes into the study, both the changes from baseline and the absolute levels of the total PI score significantly favored the heliox group. The interaction term from the analysis of variance, which compares changes from baseline, was also significant, confirming that more change had taken place in the heliox group compared with the oxygen group.

Ten (67%) patients in the heliox group were discharged from the ED compared with 5 (33%) children in the oxygen group ($P = .07$). Three of the 10 patients in the heliox group who were discharged from the ED after <240 minutes were discharged at 3 hours, and 2 of 5 patients in the oxygen group who were discharged from the ED after <240 minutes were discharged at 3 hours. Eleven (73%) patients in the heliox group were discharged from the hospital in <12 hours compared with 5 (33%) in the conventional group ($P < .05$).

Among all children discharged from the hospital, no child returned to the ED or had an unscheduled visit to their primary care physician as determined by 24-hour and 7-day telephone follow-up. All patients had successful follow-up by pager, cell phone, or best contact telephone number.12 All patients tolerated their oral corticosteroids, and none received parenteral corticosteroids in the ED. One patient required a 60:40 helium/oxygen mixture for 1 hour before titration to 70:30 helium/oxygen to maintain adequate oxygenation.

**DISCUSSION**

This is the first prospective, randomized, single-blind study to report the use of heliox-driven albuterol nebulization in moderate to severely ill pediatric asthmatic patients. Including children younger than 6 years necessitated the use of the PI score as the primary outcome measure as opposed to pulmonary-function tests. A 70:30 helium/oxygen mixture was chosen instead of 80:20 helium/oxygen to avoid the hypoxemia observed by prior investigators.13

This study found that the administration of nebulized continuous albuterol by heliox to moderately to severely ill asthmatic children, early in the course of their ED care, resulted in a substantial clinical improvement as indicated by the PI score. In addition, we observed a significant statistical difference in unblinded discharge rates at the 12-hour treatment point between the heliox and oxygen groups. Although we observed no statistically significant difference in ED discharge or PICU admission rates, a trend was noted toward ED discharge in the heliox group. The study lacked adequate power to evaluate these secondary outcome measures.

Barach14 first used a heliox mixture for treating asthma patients in 1935. Helium has a lower density and higher kinetic viscosity than air and oxygen. Heliox-based delivery of an aerosol medication may produce beneficial effects through several mechanisms. The lower density of heliox results in a lower propensity for the gas flows to become transitionally or fully turbulent.9 Turbulent flows result in higher flow resistance, and turbulence patterns may adversely affect aerosol deposition within the airways and lungs. The most likely effect explaining the beneficial outcomes associated with heliox occurs in the conducting airways that provide the dominant com-

### TABLE 2. Baseline Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Heliox Group ($n = 15$)</th>
<th>Oxygen Group ($n = 15$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age, y, mean (SD)</td>
<td>7.54 (3.16)</td>
<td>7.20 (5.58)</td>
<td>.42</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>5 (33)</td>
<td>10 (67)</td>
<td>.07</td>
</tr>
<tr>
<td>Patient race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>9 (60)</td>
<td>9 (60)</td>
<td>.58</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>5 (33)</td>
<td>6 (40)</td>
<td>.71</td>
</tr>
<tr>
<td>$\beta_2$-agonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 h before, n (%)</td>
<td>7 (47)</td>
<td>8 (53)</td>
<td>.72</td>
</tr>
<tr>
<td>24 h before, n (%)</td>
<td>13 (87)</td>
<td>13 (87)</td>
<td>1.00</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the past, n (%)</td>
<td>14 (93)</td>
<td>12 (80)</td>
<td>.14</td>
</tr>
<tr>
<td>In the past 4 wk, n (%)</td>
<td>3 (20)</td>
<td>2 (13)</td>
<td>.22</td>
</tr>
<tr>
<td>In the past 7 d, n (%)</td>
<td>0 (0)</td>
<td>2 (13)</td>
<td>.14</td>
</tr>
<tr>
<td>Mean PI score at entry</td>
<td>10.7 (1.5)</td>
<td>9.7 (1.5)</td>
<td>.11</td>
</tr>
<tr>
<td>Mean initial oxygen % saturation on room air</td>
<td>92.3</td>
<td>92.3</td>
<td>.67</td>
</tr>
<tr>
<td>Inhaled steroids, n (%)</td>
<td>5 (33)</td>
<td>8 (53)</td>
<td>.27</td>
</tr>
<tr>
<td>Other controller therapies, n (%)</td>
<td>3 (20)</td>
<td>7 (46)</td>
<td>.12</td>
</tr>
<tr>
<td>Mean previous hospitalizations, n</td>
<td>2.7</td>
<td>1.87</td>
<td>.46</td>
</tr>
</tbody>
</table>
ponent of flow resistance for the lungs as a whole and where conditions of turbulence or near turbulence are likely under most any conditions. In turbulent or near-turbulent flow regions, flow resistance decreases with decreased gas density. The lower resistance in the conducting airways associated with heliox flows will provide increased ventilation to the peripheral lung. Entrained aerosols are also likely to be conveyed deeper into the lung when heliox is used.

Similar to the findings of Anderson et al in adult asthma patients, Piva et al recently published radionuclide data in pediatric asthma patients that demonstrated increased pulmonary aerosol deposition with heliox. We hypothesize that both improved ventilation and the increased peripheral delivery and deposition of aerosol medication resulted in the improvement in the PI score noted in the heliox group in our study.

Most previous studies of heliox use during acute asthma exacerbations have looked at helium gas itself as a means of decreasing airway resistance, improving flow, and potentially averting respiratory failure or facilitating mechanical ventilatory end points. These studies have looked at the following outcome measures: peak exploratory flow rate; pulvus paradoxus; peak airway pressure during mechanical ventilation; arterial partial pressure of carbon dioxide and pH during a time when the patient was actively breathing heliox; and ventilatory parameters. It is important to note that these studies examined the effects of heliox to temporize respiratory distress. These studies did not use heliox to drive albuterol therapy.

Recently, variable results were found in adult asthmatics with heliox-driven albuterol nebulization. Limitations of these studies included 60- to 90-minute durations of heliox therapy as well as variable dosage and administration of systemic corticosteroids. It is important to note that our study found significant differences in the PI after 2 hours of therapy. Thus, our longer heliox-driven albuterol therapy may have led to our differing results.

Our study had several limitations. First, our study was powered to detect a significant and clinically important difference in the PI. However, it was not powered to detect a difference in ED discharge rates, an end point that would require a much larger sample size.

Second, the lack of blinding of the patient may have affected the PI score. A patient’s sense of dyspnea can be affected by knowing that he/she is receiving a treatment, and this knowledge can, in turn, influence respiratory rate and retractions.

Third, the lack of blinding for the attending physician who determined admission, ED discharge, and hospital discharge is another limitation. There may have been a bias to discharge ED patients treated with heliox because they had received a perceived higher level of care. Alternatively, this bias may have been offset. There may have been a bias toward admission for those patients treated with heliox based on a perception that these patients required closer monitoring after receiving a perceived higher level of therapy.

Fourth, we chose to give 15 mg/hour of continuous albuterol to all patients. This practice was in keeping with our present local asthma guideline. Weight-based albuterol dosing (0.45 mg/kg per hour) would have led to doses for children <33.3 kg that were less than that indicated in our present asthma guidelines. Five patients in the oxygen group were <33.3 kg (versus 4 patients in the heliox group).

Theoretically, these patients in the oxygen group received a higher dose per weight than the heliox group, which could have led to a bias toward the PI showing less or no benefit from heliox. In fact, we observed a significant improvement in PI despite this bias.

Finally, the use of face masks for delivering aerosolized medications may limit the applicability of this study to younger-aged children who may not tolerate face masks. In our study, 1 patient (2.05 years of age) did not tolerate his face mask, leading to exclusion from the study. This patient reflects our own clinical experience that there is variable toleration of face masks by children between 2 and 5 years of age.

Finally, the use of heliox as a driving gas has been shown to affect the size and output rate of nebulized aerosols when compared with air or oxygen. Here we attempted to match the drug-output rate from the nebulizers by increasing the heliox flow rates until the delivery rates were similar to those attained with oxygen. No attempt was made to measure or match the size of the aerosols. Differences in aerosol size could potentially cause differences in the deposition patterns of the aerosols.

Our small investigation demonstrated a statistically and clinically significant short-term improvement in respiratory function among a small group of patients with acute asthma exacerbations compared with controls. These results will require confirmation with an expanded focus on blinded, short-term clinical outcomes including ED disposition, ED length of stay, and complications. Our findings suggest that heliox may serve a future role as an adjunct therapy for moderate to severe asthma exacerbations in pediatric patients.

ACKNOWLEDGMENTS

This study was funded in part by an unrestricted $20,000 research grant from the Praxair Corporation. The Praxair Corporation had no role in the design, conduct, interpretation, or analysis of the study or review or approval of the manuscript. During this study, none of the investigators were paid employees or shareholders or worked as paid consultants for the Praxair Corporation.

We thank the following people for help and support in completing this study: Tracy Kim, DMD, RRT, Kendra Sikes, EIT, Bill Bryce, Paul Garvey, Brad Hagstrom, Abdul-Aziz Rashad, PhD, Mark Nowartarski, Richard Scarfone, MD, Ray Karasic, MD, Eric Keuffel, MPH, and Hugh Parrish; Children’s Hospital of Pittsburgh PICU and emergency department respiratory therapy staff; Rica Bonomo, Brian Bucher, Jessica Colburn, Tara Cronin, Gretchen Dickson, Pavan Gupta, Steve Guyton, Lindsay Johnston, Adam Kennah, Jennifer Lamb, Brett Mencich, Ty Mulhly, Kendra Papson, Amal Puswella, Peggy Tchao, and Kathy Wheeler (University of Pittsburgh medical students); and Steve Cico, MD, Noel Zuckerbraun, MD, Dave Barrett, MD, Robert Hickey, MD, Richard Saladino, MD, Sonia Singh, MD, Sylvia Garcia, MD, Sandy Herr, and...
MD, Mary Clyde Pierce, MD, and Ev Vogeley, MD (Children’s Hospital of Pittsburgh emergency department staff).

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FEWER A’S, AND PRINCETON CALLS IT PROGRESS

“Princeton University significantly reduced the number of A’s it gave out last year, according to a report released yesterday by the university, but it still wants to do more. Roughly 41 percent of the grades given in undergraduate courses last year were A-pluses, A’s or A-minuses, down from 46 percent the previous year and 48 percent the year before that. In April 2004, the Princeton faculty set a goal of 35 percent. The school year that ended in May was the first year under the policy. . . . Princeton was not alone in its generous grading, she said. A Princeton survey of the eight Ivy League colleges plus Stanford, M.I.T and University of Chicago, made before Princeton adopted its tougher grading policy, found that A’s accounted for 44 percent to 55 percent of their undergraduate grades.”


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Helium/Oxygen-Driven Albuterol Nebulization in the Treatment of Children With Moderate to Severe Asthma Exacerbations: A Randomized, Controlled Trial

In K. Kim, Erin Phrampus, Shekhar Venkataraman, Raymond Pitetti, Al Saville, Timothy Corcoran, Ed Gracely, Nicole Funt and Ann Thompson

*Pediatrics* 2005;116;1127
DOI: 10.1542/peds.2004-2136