Heliox and Forward-Leaning Posture Improve the Efficacy of Nebulized Bronchodilator in Acute Asthma: A Randomized Trial

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BACKGROUND: Heliox and forward-leaning posture (torso inclined forward at 50–60° with the elbows resting on the thighs) are adjuncts in the administration of nebulized bronchodilator to patients with acute asthma. METHODS: We randomized 59 patients who presented to the emergency department in severe asthma crisis, into 4 treatment groups: nebulized bronchodilator + oxygen; nebulized bronchodilator + oxygen + forward-leaning posture; nebulized bronchodilator + heliox; and nebulized bronchodilator + heliox + forward-leaning posture. Before and after the bronchodilator treatments the subjects were seated with torso erect, breathing room air. Each subject received 2 doses, 20 min apart, of nebulized fenoterol (2.5 mg) plus ipratropium bromide (0.25 mg) in 3 mL of 0.9% saline, delivered with a semi-closed valved aerosol reservoir. The nebulizer was run with oxygen or 80:20 heliox. The post-treatment pulmonary function tests were performed 15 min after the second nebulization. The group's mean age was 35.1 ± 13.6 y, and there were 20 men and 39 women. RESULTS: The oxygen + forward-leaning-posture group had a greater FEV_1 improvement than the oxygen group (59% vs 38%, $P = .02$). The heliox + forward-leaning-posture group had a greater FEV_1 improvement than the oxygen group (103% vs 38%, $P = .001$) and the heliox group (103% vs 42%, $P = .03$). The heliox group had greater reduction in respiratory rate than the oxygen group ($P = .03$). The heliox + forward-leaning-posture group had significantly greater peak expiratory flow improvement than any of the other groups. CONCLUSIONS: Heliox plus forward-leaning posture during bronchodilator nebulization improves bronchodilator efficacy in patients with severe acute asthma. (ClinicalTrials.gov registration NCT00922350). *Key words: asthma; heliox; helium; bronchodilator; posture; respiratory muscles.* [Respir Care 2011;56(7):947–952. © 2011 Daedalus Enterprises]

Introduction

Short-acting bronchodilators are the preferred medication to relieve bronchospasm in patients with acute asthma.[1,2] Heliox is a mixture of helium and oxygen that reduces air-flow turbulence, compared to air or oxygen.[3-6]

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The use of heliox in asthma treatment was first reported in 1935.[7] However, few controlled studies have been carried out concerning heliox's impact on hospitalization in patients with acute asthma who do not respond to traditional treatment.

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Acute expiratory air-flow obstruction during asthma exacerbation causes lung hyperinflation, which increases the work of breathing and the load on the inspiratory muscles, putting them at a mechanical disadvantage.[8,9] Studies of postures and their relationship to that mechanical disadvantage[10,11] suggest that the influence of posture is mainly on the position of the diaphragm, increasing the tension in muscles such as the abdominals and the effect gravity has on them.[10] We studied the effect of forward-leaning posture and heliox as adjuncts to bronchodilator administration in patients with acute asthma crisis in our emergency department.

Methods

This study was approved by our human research ethics committee and conducted in the emergency department of Professor Barros Lima Hospital, Recife City, Brazil. All subjects gave written informed consent.

Subjects

We studied a random sample of 59 subjects, ages 18–65 years, who presented to our emergency department with severe asthma crisis. We calculated our sample size for a 90% power with an α of .05 and a β of .10. Our sample-size calculation was based on our pilot study that found a 25% better peak expiratory flow (PEF) improvement in patients who used forward-leaning posture, and a report by Ho et al, who found a 30% better PEF improvement in patients who received bronchodilator via heliox than via oxygen.[12]

We assessed the asthma exacerbations per the Global Initiative for Asthma system, in which an FEV_1 of $\leq 60\%$ of predicted is a "severe" exacerbation.[1] Our inclusion criteria were asthma history of $>$ 1 year, and duration of current asthma exacerbation $<$ 7 days. Our exclusion criteria were: unable to understand or perform spirometry maneuvers; smoking history of $>$ 100 cigarettes/year in the last 3 years; other pulmonary comorbidities; upper-airway infection; cardiac insufficiency; heart rate $>$ 150 beats/min; systolic pressure $<$ 90 mm Hg or $>$ 150 mm Hg; pregnancy; and inability to maintain the torso inclined forward.

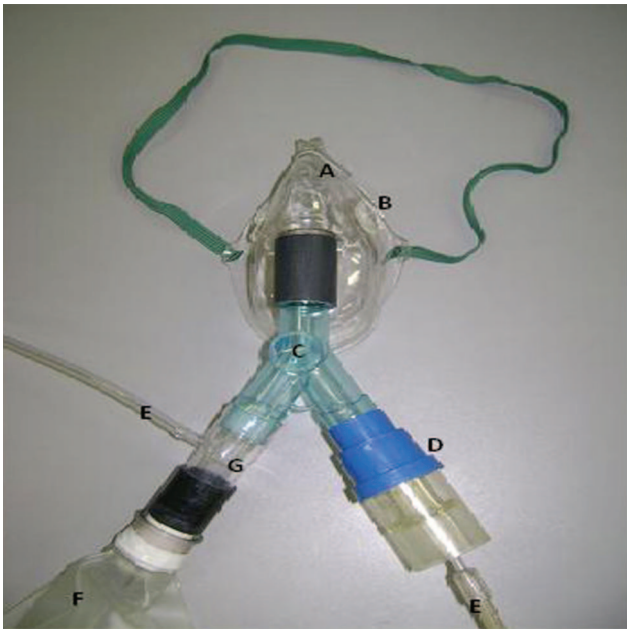

Fig. 1. Nebulization circuit. A = face mask. B = Exhalation valve. C = Y-piece. D = Nebulizer. E = Nebulizer power gas supply (oxygen or heliox). F = Bag reservoir. G = Connector (3 cm).

Procedure

The patients were randomly assigned into 4 groups:

- Nebulizer driven with oxygen, and torso erect during bronchodilator administration (oxygen group)
- Nebulizer driven with oxygen, and forward-leaning posture during bronchodilator administration (oxygen + forward-leaning-posture group)
- Nebulizer driven with heliox, and torso erect during bronchodilator administration (heliox group)
- Nebulizer driven with heliox, and forward-leaning posture during bronchodilator administration (heliox + forward-leaning-posture group)

We performed block randomization with a computerized randomization method.

Figure 1 shows the nebulization system we used, which included a transparent mask with exhalation valves, a Y-piece, a nebulizer (AirLife Misty-Neb, Baxter, Valencia, California), a 2.5-L reservoir bag, and a one-way valve. We used 80:20 heliox. The flow to the nebulizer and reservoir was 8 L/min with 100% oxygen, or 11 L/min with heliox, through an oxygen flow meter. The heliox flow was calculated based on a correction factor of 1.8.[13]

All the patients received intravenous corticosteroids (5 mg/kg hydrocortisone) before randomization. All the subjects received 2 nebulizations, 20 min apart, of fenoterol (2.5 mg) plus ipratropium bromide (0.25 mg), in 3 mL

of 0.9% saline solution. Nebulization time to end of aerosol generation was approximately 10 min. Before and after the nebulizations, all the subjects were seated with torso erect and breathing room air. The post-treatment pulmonary function tests were performed 15 min after the second nebulization. The typical time from protocol initiation to final assessment was 55 min.

At admission we conducted spirometry (MicroLoop portable spirometer, Cardinal Health, Dublin, Ohio), measured vital signs and S_{pO_2} (MD300-D pulse oximeter, Parker Healthcare, Mitcham, Victoria, Australia), and asked the patient to rate his or her dyspnea on the Borg dyspnea scale. For 15 min after the second nebulization the patient sat erect and breathed room air, then we re-measured all the variables. In each spirometry session the patient performed 3 spirometry maneuvers, and we recorded the highest FEV_1 and PEF values, in accordance with the American Thoracic Society guidelines.[14]

Our primary outcomes were percentage improvement in FEV_1 and PEF. The secondary outcomes were percentage decrease in respiratory rate, heart rate, and S_{pO_2}.

In the 2 forward-leaning-posture groups, during nebulization the subjects were instructed to maintain their torso inclined forward 50–60°, with the elbows resting on the thighs. We measured the inclination angle from the anterior axillary line to the lateral epicondyle of the femur. After nebulization these subjects were instructed to resume the erect sitting posture. The other 2 groups maintained the erect posture during nebulization.

We used a double-blind procedure so that the clinicians did not know whether the patient was receiving oxygen or heliox. The patients were not informed of which gas was being administered, and they were instructed to remain silent during and for 2 min after each nebulization, because heliox temporarily modifies vocal tone. All the data were analyzed by a researcher blinded to which gas was used during nebulization.

Statistical Analysis

We analyzed the distribution pattern of the sample with the Kolmogorov-Smirnov and Levene tests. We compared the groups with analysis of variance and the Tukey post hoc test. We applied the Kruskal-Wallis and Mann-Whitney tests with variables that had non-normal distribution. We conducted the analysis with statistics software (SPSS 13.0, SPSS, Chicago, Illinois), and used a confidence interval of 95% and significance level of $P < .05$.

Results

We assessed 101 patients for eligibility (Fig. 2). Table 1 shows the cohort's baseline characteristics. Table 2 shows the FEV_1 data. FEV_1 improvement was greater in the oxygen + forward-leaning-posture group than in the oxygen group. FEV_1 improvement was also greater in the heliox + forward-leaning-posture group than in the oxygen group or the heliox group. The heliox + forward-leaning-posture group had a greater FEV_1 improvement than the oxygen + forward-leaning-posture group, but this difference was not significant ($P = .06$).

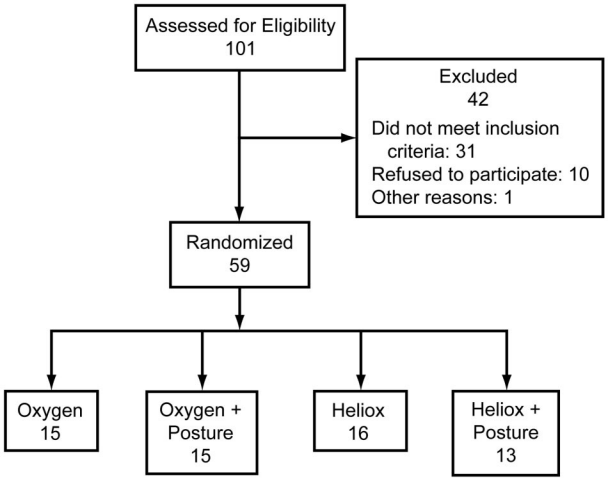

Fig. 2. Flow chart.

Figure 3 show the PEF improvements. There was a greater respiratory-rate reduction in the heliox group than in the oxygen group (34 ± 1% vs 16 ± 1%, $P = .03$). There was no statistically significant improvement for patients in the heliox group, compared to other groups, when we evaluated the spirometry values. There were no significant differences between the 4 groups in Borg dyspnea score, heart rate, or S_{pO_2} in any of the treatments.

Discussion

To our knowledge, this is the first study to analyze the influence of torso orientation and heliox on the effect of bronchodilator in patients with acute asthma in an emergency department. The combination of forward-leaning posture and heliox improved PEF more than did oxygen-driven or heliox-driven nebulization alone, without forward-leaning posture.

Conflicting results about the effects of heliox on bronchodilators are found in the literature. Our findings are similar to those of Henderson et al,[15] who found no difference in FEV_1 or PEF in asthma patients after heliox-driven bronchodilator, in comparison with oxygen. Similar results were reported by Rose et al[16] in patients with asthma in the emergency department.

Contrasting results were described by Bag et al,[17] who found better FEV_1, forced vital capacity, and PEF improvement with heliox-driven nebulization than with oxygen-driven nebulization. However, those results were from

Table 1. Baseline Characteristics of Patients With Acute Asthma (n = 59)*

	Oxygen	Oxygen + Forward-Leaning Posture	Heliox	Heliox + Forward-Leaning Posture	P
Age (y)	30.3 ± 10.9	38.5 ± 13.9	35.9 ± 16.0	36.0 ± 12.0	.06
Male/female (no.)	4/11	6/9	6/10	4/9	.07
Body mass index (kg/m^2)	24.5 ± 3.8	23.8 ± 4.5	25.1 ± 5.1	24.0 ± 3.9	.06
Heart rate (beats/min)	85 ± 16	94 ± 16	87 ± 15	92 ± 22	.08
Respiratory rate (breaths/min)	24 ± 4	26 ± 6	29 ± 5	29 ± 6	.07
S_{pO_2} (%)	97 ± 2	95 ± 3	96 ± 3	95 ± 2	.08
FEV_1 (L)	1.52 ± 0.69	1.28 ± 0.74	1.51 ± 0.69	1.19 ± 0.54	.06
FEV_1 (% predicted)	45 ± 13	35 ± 14	46 ± 17	40 ± 15	.07
PEF (L/s)	2.12 ± 1.04	2.09 ± 1.34	2.11 ± 1.14	1.62 ± 0.57	.08
PEF (% predicted)	30 ± 10	27 ± 13	29 ± 16	20 ± 7	.06
Borg dyspnea score	3.0 ± 1.2	3.9 ± 2.1	3.3 ± 1.2	4.0 ± 2.3	.07

* All values except male/female are mean ± SD.
PEF = peak expiratory flow

Table 2. Post-Treatment FEV_1 Improvement

	Oxygen	Oxygen + Forward-Leaning Posture	Heliox	Heliox + Forward-Leaning Posture
FEV_1 improvement, median (IQR), %	38 (27–45)	59 (27–79)*	42 (9–51)	103 (21–120)†‡

* P = .02 for oxygen vs oxygen + forward-leaning posture.
† P = .001 for heliox + forward-leaning posture vs oxygen.
‡ P = .03 for heliox + forward-leaning posture vs heliox.

patients with stable asthma, which may explain their divergence from the present study. Kress et al[18] observed better FEV_1 increase in acute-asthma patients with heliox-driven nebulization of albuterol than with standard treatment. This may not have been found in our study because the patients studied by Kress et al[18] had more severe asthma (baseline FEV_1 was lower in both groups than in our study). Those 2 studies also used methods different from ours.

Our heliox group had a better decrease in respiratory rate than our oxygen group. Few randomized controlled trials have studied respiratory rate in emergency-department asthma patients treated with heliox-driven bronchodilator. Rose et al[16] carried out a randomized study with patients in asthma exacerbation and found no respiratory-rate difference between the 2 groups, which contradicts our results. A possible explanation may be that they used a lower helium concentration than we did, and an open breathing system that entrained room air.

Our findings corroborate those of Kress et al,[18] who observed better respiratory-rate reduction in acute-asthma patients with 80:20 heliox-driven bronchodilator nebulization than with oxygen-driven nebulization. This respiratory-rate decrease may be explained by helium's low density, which reduces air turbulence and therefore reduces the pressure necessary to generate a given air flow, and thus reduces the work of breathing.[18]

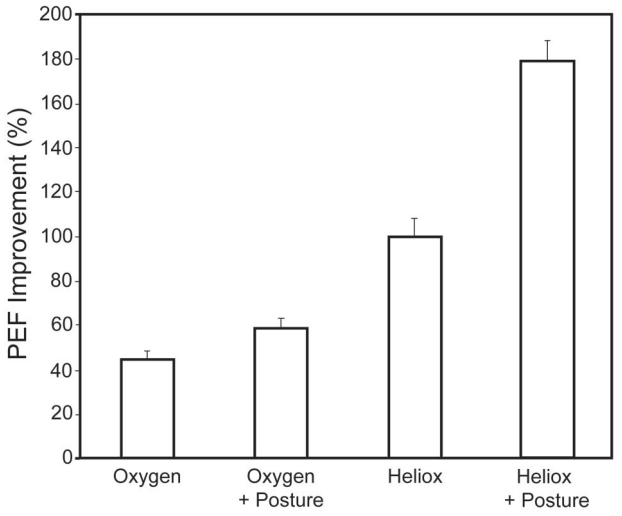

Fig. 3. Post-treatment percentage improvement in peak expiratory flow. All the differences are statistically significant: P = .04 for oxygen versus heliox + posture; P = .03 for oxygen + posture versus heliox + posture; P = .02 for heliox versus heliox + posture.

The modified Borg dyspnea scale is applied while the patient is experiencing symptoms.[19] Only one previous study[16] has employed the Borg dyspnea scale in acute-

asthma patients divided into heliox-driven and oxygen-driven nebulization (of albuterol) groups. With heliox-driven nebulization Rose et al[16] found better modified Borg dyspnea score improvement after 2 hours, and a more lasting effect. We found no significant differences in Borg dyspnea score at any point. However, our final measurements were carried out approximately 55 min into treatment, which might explain this divergence between the 2 studies.

We know of no other studies on forward-leaning posture during nebulization in acute-asthma patients. However, some studies have correlated respiratory pattern in asthma patients and the influence of the respiratory muscles, and some studies have investigated the interaction of posture and the respiratory muscles. Lung hyperinflation appears to be a determining factor in the worsening of acute bronchospasm.[20-22] Functional residual capacity is dynamically determined in acute asthma, where expiration is actively interrupted by the contraction of the inspiratory muscles.[21,22] Hyperinflation is maintained by the tonic contraction of these muscles. Diaphragm activity decreases in a brief expiration, while abdominal muscles are recruited.[20]

De Troyer[23] explained that alterations in abdominal muscle contraction occur in response to posture changes and the proprioceptive influence of these muscles. Tonic contraction of these muscles plays a predominant role in regulating the expiratory volume. De Troyer also pointed out that abdominal muscle contraction promotes cephalad displacement of the diaphragm and stretches the diaphragm's fibers. Consequently, the diaphragm starts contracting during inspiration with maximum stretch, which increases its ability to generate pressure, which may reduce the work of breathing.

Liu et at[24] studied the effects of gravitational force on the thoracoabdominal system. They concluded that the weight of the chest cage and shoulders determines the gravitational force in this system and acts as an "expiratory force." Therefore, the forward-leaning posture we used in this study shifts the center of gravity and optimizes expiration.

In a study with 27 healthy adults, Kera and Maruyama[10] concluded that changes in respiratory muscle strength related to posture are caused by alterations in intra-abdominal pressure. In a more recent[11] study, the same authors investigated postural influence on the expiratory activity of abdominal muscles in 15 young adults. Muscle activity was evaluated with electromyography, with the subjects in seated, standing, and supine positions, and with the elbows resting on the thighs. Abdominal muscle activity differed in the different positions, although the external oblique muscles were more active when the torso was inclined with the elbows on the thighs. Thus, the forward-leaning posture may benefit patients with obstructive diseases, and the accessory muscles stabilize when the torso inclines, which optimizes inspiration.

When the functional residual capacity is above normal, the inspiratory load is difficult to maintain. Patients with asthma show an increase in functional residual capacity and resistive load during inspiration and expiration. Heliox may improve this condition when it can reduce functional residual capacity. This gives the respiratory muscles a mechanical advantage while simultaneously decreasing resistive load.[25] Mechanical advantage is enhanced when the torso is forward-inclined because expiratory muscle function improves and abdominal pressure increases. This explains the improved spirometry values when heliox is combined with forward-leaning posture. These spirometric values, represented by PEF and FEV_1, showed different behaviors in this study, which can be attributed to 2 factors. First, PEF is more effort-dependent than FEV_1. The second factor is linked to the difficulty of making a longer expiration to obtain FEV_1 in a patient with severe acute asthma.

We found no significant differences in heart rate or S_{pO_2} between our groups, whereas Kress et al[18] found higher heart rate with heliox-driven nebulization (of albuterol) than with oxygen-driven nebulization. Kress et al suggested that this fact was owed to the probable increase in pulmonary albuterol deposition with heliox. Rose et al[16] studied the behavior of S_{pO_2} in a study similar to that of Kress et al,[18] and, as in our study, found no significant S_{pO_2} difference between the heliox-driven and oxygen-driven nebulization groups. This can be considered a positive finding for low-oxygen heliox, when compared to isolated oxygen, presuming an improved ventilation-perfusion ratio with heliox.

Limitations

We used a handheld spirometer. Even if the patients inhaled room air prior to attempting pulmonary function testing, the residual heliox in the lungs could have given spurious values. This may explain why we found no significant spirometric differences between our heliox and oxygen groups. We did not collect data about the need for intubation or hospital stay. Regarding the number of intubations, none of our patients required intubation until after the intervention. It will be important in future studies to evaluate the longer-term effects of heliox and oxygen (eg, 4–6 hours after initiating therapy). The present study also lacked quantification of the penetration of radiation activity in lung tissue, and aerosol particle size.

Conclusions

To our knowledge, this is the first study to find that the combination of heliox and forward-inclined torso improves

post-nebulization FEV_1 and PEF in patients with severe acute asthma. There was much greater improvement with heliox-driven than with oxygen-driven nebulization. However, further studies are needed to determine to what extent this response improves important clinical outcomes such as a emergency-department stay and hospitalization rate.

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