CRITICAL CARE ALERT®

A monthly update of developments in critical care and intensive care medicine

Thomson American Health Consultants Home Page—http://www.ahcpub.com

CME for Physicians—http://www.cmeweb.com; CE for Nurses—http://www.ceweb.com

THOMSON
AMERICAN HEALTH CONSULTANTS

INSIDE

Should We Use Nitric Oxide with High-Frequency Oscillatory Ventilation in ARDS?

ABSTRACT & COMMENTARY

THE OBJECTIVE OF THIS STUDY WAS TO PROSPECTIVELY EVALUate the oxygenation effect of inhaled nitric oxide (iNO) delivered during high-frequency oscillatory ventilation (HFOV) in patients with the acute respiratory distress syndrome (ARDS). It was a prospective observational study that enrolled 23 adult patients with ARDS who required more than 60% oxygen and had mean airway pressures of > 28 cm H_2O. Inhaled nitric oxide was initiated at a dose of 5 ppm and subsequently titrated to determine the dose (5, 10, or 20 ppm) resulting in the greatest increase in arterial oxygenation, as measured by PaO_2/FIO_2 ratio. Arterial blood gas measurements were obtained 10-15 min after initiation or any increase in iNO dosage to assess the effect on PaO_2/FIO_2. Arterial blood gases and ventilator settings were recorded at 4 time points: conventional ventilation just before initiating HFOV, HFOV just before initiating iNO therapy, 30 min after the optimal dose of iNO, and 8-12 h after starting iNO. Oxygenation index and PaO_2/FIO_2 were calculated at the same time intervals.

At 30 min after iNO initiation, 19 (83%) of the patients had a significant increase in arterial oxygenation, as defined by > 20% increase in PaO_2/FIO_2. The mean change in PaO_2/FIO_2 at 30 min was 38%. In these 19 patients, PaO_2/FIO_2 was highest at 20 ppm iNO in 4 patients, at 10 ppm in 8 patients, and at 5 ppm in 7 patients. Compared with baseline measurements, PaO_2/FIO_2 improved significantly at both 30 min (112 ± 59 vs 75 ± 32 mm Hg; $P = 0.01$) and 8-12 h after initiation of nitric oxide therapy (146 ± 52 vs 75 ± 32 mm Hg; $P < 0.0001$). In addition, oxygenation index ([FIO_2 × mean airway pressure × 100]/PaO_2) was reduced at 8-12 h compared with baseline measurements (26 ± 13 vs 40 ± 17; $P = 0.08$). Mehta and colleagues concluded that iNO delivered at doses of 5-20 ppm during HFOV increases PaO_2/FIO_2 and may be a safe and effective rescue therapy for patients with severe oxygenation failure (Mehta S, et al. Acute oxygenation response to inhaled nitric oxide when combined with high-frequency oscillatory ventilation in adults with acute respiratory distress syndrome. *Crit Care Med.* 2003;31:383-389.)

VOLUME 11 • NUMBER 2 • MAY 2003 • PAGES 13-24

COMMENT BY DEAN R. HESS, PhD, RRT

It is well known that iNO produces an improvement in PaO_2 (albeit short-lived) in many patients with ARDS.[1] It is likewise known that HFOV can similarly improve PaO_2 in some patients with ARDS.[2-4] Moreover, it has been shown in infants that the combination of iNO and HFOV improves oxygenation more than either therapy used alone.[5] Accordingly, the results of this study are not entirely surprising. However, this study falls short of convincing me to adopt this therapy into my practice. I don't believe that this study provides convincing evidence that every ICU must have available iNO and a high-frequency oscillatory ventilator to treat their patients with severe ARDS.

There are several significant methodologic problems with this study. First of all, the patients were not randomized. Placebo-controlled, randomized-controlled trials of the use of iNO in patients with ARDS have failed to show a survival benefit (despite short-term improvements in oxygenation).[6-9] Second, the patients did not have a trial of nitric oxide while receiving conventional ventilation. Perhaps the oxygenation response with iNO during conventional ventilation would have been as good (or perhaps even better) than it was with HFOV. It is of interest to note that Mehta et al found no significant improvement in PaO_2/FIO_2 or oxygenation index when patients were switched from conventional ventilation to HFOV. This raises the obvious question, why go to the trouble of using high-frequency ventilation in the first place? Third, Mehta et al use a physiologic outcome (oxygenation) to judge success. Short-term physiologic outcomes have increasingly been recognized as poor surrogates for patient-important outcomes such as survival.[10] The hospital survival rate in this study was only 30%. Mehta et al might argue that these were very ill patients, but the fact remains that we have no idea what the survival rate would have been without the use of iNO and HFOV.

One concern in this study is the high incidence of pneumothorax (22%). This is much higher than what is typically observed in patients with ARDS. For example, the incidence of barotrauma in the ARDSnet study was only 10%.[11] Because barotrauma has not been reported with the use of iNO, I speculate that the high incidence of pneumothorax in this study was related to the high mean airway pressure associated with HFOV.

Mehta et al conclude that the combination of iNO and HFOV may be a safe and effective rescue therapy for patients with severe ARDS. I have always been confused by the meaning of "rescue therapy." What does this mean? Generally, rescue therapy is the use of an unproven therapy for patients who, in the clinical opinion of those providing care, are failing conventional therapy. If the patient improves after the rescue therapy is initiated, this improvement is attributed to the new therapy. As is the case in this study, the survival with the rescue therapy is usually low. Although the majority of patients who receive the rescue therapy do not survive, the survival of the few is attributed to the rescue therapy. This is most curious reasoning. One might argue that the rescue therapy is ineffective because the majority of patients who receive it do not survive! Perhaps those with a good outcome survive in spite of the rescue therapy rather than because of it!

Of concern is that "rescue therapy" is often also "expensive therapy." This is particularly true of iNO and HFOV. In the United States, 4 days of iNO therapy costs $12,000 and a high-frequency oscillatory ventilator costs more than $25,000. This does not include the training costs and additional clinical demands required for the use of these therapies. In

Critical Care Alert, ISSN 1067-9502, is published monthly by Thomson American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

VICE PRESIDENT/GROUP PUBLISHER: Brenda Mooney.

EDITORIAL GROUP HEAD: Glen Harris.

MANAGING EDITOR: Robin Mason.

ASSISTANT MANAGING EDITOR: Robert Kimball.

SENIOR COPY EDITOR: Christie Messina.

MARKETING PRODUCT MANAGER: Schandale Kornegay.

GST Registration Number: R128870672.

Periodicals postage paid at Atlanta, GA.

POSTMASTER: Send address changes to *Critical Care Alert,* P.O. Box 740059, Atlanta, GA 30374.

Back issues: $38.

Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issues date.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail Address: customerservice@ahcpub.com

Editorial E-Mail Address: robin.mason@ahcpub.com

World Wide Web: http://www.ahcpub.com

Subscription Prices

United States

1 year *with* free AMA Category 1 credits: $279

(Student/Resident rate: $140)

Multiple Copies

1-9 additional copies: $206 each; 10 or more copies: $183 each.

Canada

Add GST and $30 shipping.

Elsewhere

Add $30 shipping.

Accreditation

Thomson American Health Consultants (AHC) designates this educational activity for a maximum of 28 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

This CME activity was planned and produced in accordance with the ACCME Essentials.

AHC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

AHC is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. Provider approved by the California Board of Registered Nursing, Provider Number CEP 10864, for approximately 16 contact hours.

THOMSON AMERICAN HEALTH CONSULTANTS™

Questions & Comments

Please call **Robin Mason,** Managing Editor, at (404) 262-5517 or e-mail at robin.mason@ahcpub.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Statement of Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Ms. Ball serves as a consultant to Steris Corp, IC Medical, and AMT-Coherent (Canada), is a stockholder of Steris and SLT, and is on the speaker's bureau of AORN. Dr. Pierson is on the speaker's bureau of GlaxoSmithKline, Boehringer-Ingelheim, 3-M, Bayer, and Astra Zeneca. Dr. Rubenfeld is a consultant to Eli Lilly and is involved in research with the National Institutes of Health. Drs. Baigorri, Durbin, Hess, Hoffman, Johnson, and O'Keefe report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. Drs. Crawford, Gladwin, Nanavaty, and Takezawa did not return a 2003 financial disclosure form.

these days of cost constraints in health care, it is difficult to justify expensive therapies for which there is a low level of scientific evidence. The benefit of any rescue therapy can only be determined by an appropriately designed randomized controlled trial with patient-important outcomes. All too often, anecdotally supported "rescue therapy" has later been found ineffective (or worse, harmful) when subjected to appropriately designed studies. ■

References

1. Manktelow C, et al. Physiologic determinants of the response to inhaled nitric oxide in patients with acute respiratory distress syndrome. *Anesthesiology*. 1997; 87:297-307.
2. Fort P, et al. High-frequency oscillatory ventilation for adult respiratory distress syndrome—A pilot study. *Crit Care Med*. 1997;25:937-947.
3. Mehta S, et al. Prospective trial of high-frequency oscillation in adults with acute respiratory distress syndrome. *Crit Care Med*. 2001;29:1360-1369.
4. Derdak S, et al. High-frequency oscillatory ventilation for acute respiratory distress syndrome in adults: A randomized, controlled trial. *Am J Respir Crit Care Med*. 2002;166:801-808.
5. Kinsella JP, Abman SH. High-frequency oscillatory ventilation augments the response to inhaled nitric oxide in persistent pulmonary hypertension of the newborn: Nitric Oxide Study Group. *Chest*. 1998; 114(1 Suppl):100S.
6. Dellinger RP, et al. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: Results of a randomized phase II trial. Inhaled Nitric Oxide in ARDS Study Group. *Crit Care Med*. 1998;26:15-23.
7. Lundin S, et al. Inhalation of nitric oxide in acute lung injury: Results of a European multicentre study. *Intensive Care Med*. 1999;25:911-919.
8. Michael JR, et al. Inhaled nitric oxide versus conventional therapy: Effect on oxygenation in ARDS. *Am J Respir Crit Care Med*. 1998;157:(5 pt. 1)1372-1380.
9. Troncy E, et al. Inhaled nitric oxide in acute respiratory distress syndrome: A pilot randomized controlled study. *Am J Respir Crit Care Med*. 1998;157:(5 pt. 1) 1483-1488.
10. Rubenfeld GD. Surrogate outcome measures in critical are: It's the mortality, stupid! *Critical Care Alert*. 2002;9:138-140.
11. The ARDS Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342:1301-1308.

Should Critically Ill Patients Receive Erythropoietin?

ABSTRACT & COMMENTARY

Synopsis: *In this large, randomized trial, critically ill patients who received weekly doses of recombinant human erythropoietin had higher hemoglobin levels and required fewer transfusions than placebo-treated patients.*

Source: Corwin HL, et al. Efficacy of recombinant human erythropoietin in critically ill patients. A randomized controlled trial. *JAMA*. 2002;288(22): 2827-2835.

Recombinant human erythropoietin (rHuEPO) is being heavily promoted for use in critically ill patients. This multicenter, randomized, controlled clinical trial, sponsored by the drug's manufacturer (Ortho Biotech), sought to determine whether weekly injections of rHuEPO (40,000 U) would raise hemoglobin levels in this setting and thereby reduce erythrocyte transfusions. At 65 US medical centers, Corwin and colleagues screened 33,685 ICU patients for inclusion in the study. Of these, 9674 met eligibility criteria (age 18 or older; hematocrit < 38%; anticipated ICU stay at least 3 days; and informed consent), and 1302 were randomized to receive either rHuEPO or placebo weekly for 3 doses starting on ICU day 3. All patients also received either oral or parenteral iron. Criteria for transfusion were not rigidly enforced but Corwin et al recommended a hematocrit threshold of 27% (hemoglobin 9 g/dL) in the absence of a specific indication such as bleeding or ischemia. The primary end point was the percentage of patients in each group who received any red blood cell transfusion within 28 days. Secondary end points were cumulative units transfused per patient, 28-day mortality, change in hemoglobin from baseline, and time to first transfusion or death.

The patients in the rHuEPO and placebo groups were well matched. Of the 650 patients who received rHuEPO, 328 (50.5%) received at least 1 red blood cell transfusion during the 28-day study period, as compared to 394 of the 652 placebo-treated patients (60.4%; $P < 0.001$; OR, 0.67; 95% CI, 0.54-0.83). Statistical analysis demonstrated a 19% reduction in units transfused per day alive ($P = 0.04$). The mean increase in hemoglobin concentration from baseline to final determination was significantly greater in patients who received rHuEPO (1.32 vs 0.94 g/dL; $P < 0.001$). There

were no differences in 28-day mortality (14% and 15% in rHuEPO and placebo groups, respectively) or other adverse events examined. The mean pretransfusion hemoglobin levels were 8.53 and 8.57 g/dL for the 2 groups, and 21% of patients in each group underwent transfusion at a hemoglobin level greater than 9 g/dL (hct > 27%).

COMMENT BY DAVID J. PIERSON, MD

This study shows that, under the conditions of this study, when administered weekly at a dose of 40,000 U (at a cost of about $400 per dose), rHuEPO reduces by approximately 10% the number of adult general ICU patients receiving red blood cell transfusion. A number-needed-to-treat analysis cited in an accompanying editorial[1] showed that, among patients staying in the ICU for at least 3 days, 10 patients would need to be treated with rHuEPO in order to prevent 1 patient from receiving a transfusion during the next 28 days. The study was not sufficiently powered to detect differences in survival, although the death rates (111 patients in the rHuEPO group compared with 120 patients in the placebo group) make it unlikely that even a much larger study would show such a difference.

As clinicians, what should we do with these findings? Should we prescribe rHuEPO for all patients who remain in the ICU for 72 hours and are likely to be there for several more days? Such a practice has been adopted by some of my colleagues and is certainly defensible on the basis of available evidence if avoidance of transfusion is considered an important enough goal to justify the cost.

Three points raised by Carson in the editorial cited above[1] are worth noting, however. One is that the risks associated with red blood cell transfusion in the United States in 2003 are very small. Current estimates of infection risk are 1 case of hepatitis C per 1.935 million transfused U, and 1 case of HIV transmission per 2.135 million U.[2] Although more common, such adverse effects as allergic reactions, febrile nonhemolytic transfusion reactions, and erythrocyte or leukocyte/platelet alloimmunization are not usually serious; more serious complications are both rare and more likely to be due to human error than to a problem with the blood supply.

The other points have to do with the present study and how well its results apply to our own practices. First, patients on whom the data were collected represented only 13% of those eligible: nearly two-thirds of patients meeting the entry criteria were not approached by Corwin et al for inclusion, and half of all patients or surrogates asked to participate declined to do so. This raises concerns about generalizability. I would have to take it on a certain amount of faith that the study's results would be the same if I applied the same regimen across the board to my patients that met the listed entry criteria. And, second, Corwin et al did not control transfusion practice, and the clinicians managing the patients applied a fairly liberal (by current standards) hemoglobin threshold of about 8.5 g/dL. According to several recent studies, it appears to be safe to use a transfusion threshold of around 7 g/dL in the absence of severe cardiac disease or other specific contraindication. The transfusion reductions achieved in this study were not large, and might thus have been achievable simply by applying this lower transfusion cut-off.

The availability of rHuEPO is an important advance, which has greatly benefited some patient populations. In the ICU its role remains unclear, however, because of cost considerations, differences of opinion about the indications and hazards of red blood cell transfusion, and uncertainty about which patients might benefit most from its use.

References

1. Carson JL. Should patients in intensive care units receive erythropoietin? *JAMA*. 2002;288(22): 2884-2886.
2. Dodd RY, et al. Current prevalence and incidence of infectious disease markers and estimated window-period risk in the American Red Cross blood donor population. *Transfusion*. 2002;42:975-979.

Special Feature

Heliox in Acute Severe Asthma

By David J. Pierson, MD

ALVAN BARACH, WHO PIONEERED THE CLINICAL USE of oxygen, was also the first investigator to treat acute asthma by having the patient breathe a mixture of helium and oxygen. In 4 adult asthmatics, Barach demonstrated a reduction in dyspnea after just a few breaths of the helium-oxygen mixture, now known as heliox.[1] This therapy received little subsequent attention until the 1980s, but in the last decade there has been a resurgence of both publications and clinical use of heliox in acute severe asthma.[2] Although I know of no national data, my impression is that it is currently much more widely used, especially in emergency departments, than at any time in the past. In addition to its use

via mask in nonintubated patients with acute asthma, there are also a number of reports of the administration of heliox during mechanical ventilation in both status asthmaticus and severe chronic obstructive pulmonary disease. In this brief review I summarize the arguments in favor of using heliox in asthma, discuss the findings of several recent comprehensive literature reviews, and offer my personal opinion on how heliox fits in with the other available therapies for acute severe asthma.

What is Heliox and What Does it Do?

Helium is an inert, colorless, odorless gas occurring naturally in the atmosphere. Other than hydrogen, it is the least dense gas known, which accounts for its use in weather balloons and blimps. Its medical interest also arises from its low density. Pure helium is only one-seventh as dense as nitrogen but slightly more viscous. The addition of 20% oxygen increases the density to one-third that of air, and it is doubtful whether mixtures much more than 30% oxygen are appreciably different from their nitrogen counterparts. Heliox is most commonly used in mixtures of 80:20 or 70:30 helium:oxygen and is available in large compressed-gas cylinders (H tanks). The physical properties of heliox decrease the tendency for gas turbulence in obstructed airways, tending to make flow more laminar and hence more energy-efficient.

Why Might Heliox be Beneficial in Acute Severe Asthma?

As shown in the Table, there are several theoretical reasons why breathing heliox might be physiologically advantageous for a patient with acute severe asthma in comparison to breathing a mixture of nitrogen and air. Most important is probably the effect on resistance in the airways. With more laminar flow, less resistive work is required to move air in and out of the lungs, and the pressures that must be generated to do so are decreased. As a result, peak inspiratory and expiratory flows are increased, and less ventilatory muscle work is required for a given minute ventilation. Heliox has also been demonstrated to reduce pulsus paradoxus in acute asthma. All these effects would tend to relieve fatigue and respiratory distress and could theoretically reduce the need for mechanical ventilation.

Increased airway resistance promotes air trapping and dynamic hyperinflation in acute asthma, and heliox should have a beneficial effect on these as well, with an attendant reduction in work of breathing and relief of dyspnea. Studies have also shown that the deposition of aerosols in the airway is augmented by the presence of helium in the breathing mixture.[3] This in turn could lead to greater bronchodilator effect and more rapid improvement in airway function in acute severe asthma.

What Do Heliox's Advocates Say?

There are thus a number of sound theoretical reasons why breathing heliox should be beneficial not only in acute asthma but also in COPD as well as epiglottitis, croup, and other forms of upper airway obstruction. Early case series suggested that fewer patients presenting to the emergency department (ED) with acute severe asthma required hospitalization, and that intubation could perhaps be avoided, with heliox delivered by mask. There were also reports of dramatic improvement in airway pressures and arterial blood gases in intubated, ventilated patients. As a result, heliox has become a standard component of therapy in some EDs, and many clinicians advocate its use when initial management with bronchodilators and corticosteroids does not result in prompt improvement.

Table

Potential Benefits of Heliox Administration in Acute Severe Asthma

Benefit	Mechanism	Potential Implications
Decreased resistive work of breathing	Reduced turbulent flow and increased laminar flow in airways	Increased peak expiratory flow; Decreased pulsus paradoxus; Decreased ventilatory muscle; fatigue Avoidance of need for mechanical ventilation;
Reduced dynamic hyperinflation	More complete exhalation (to lower lung volume)	Decreased work of breathing; Decreased dyspnea
Improved airway distribution of aerosols	Increased laminar flow; Increased peripheral deposition of particles	Increased effectiveness of bronchodilators

What Does the Evidence Say?

Heliox can indeed improve bronchodilator delivery in acute asthma. Recently, a randomized, controlled trial of albuterol nebulization via heliox vs oxygen in 45 patients presenting to the ED with acute asthma[4] showed more effective drug administration with the former. The patients were given 3 nebulizer treatments using the same amount of drug. That more drug reached the lower respiratory tract with heliox was shown by the findings of significantly greater improvement in spirometry (32% vs 15% improvement in forced expiratory volume in the first second [FEV_1] after the first nebulizer treatment) and significantly higher heart rates.

The study just mentioned did not address the effect of heliox on patient outcomes, and here the literature is much less impressive. A Cochrane Review of literature published through September 2001[5] found 4 randomized controlled trials that met Rodrigo and associates' *a priori* inclusion criteria, 3 studies involving adults, and a fourth including only children, with a total of 288 patients. The main outcome in all 4 trials was 1 or more measures of pulmonary function (mainly peak expiratory flow [PEF]), and systematic review of the pooled data revealed no significant differences. Comparisons of data from adults vs children, high vs low heliox dose, and high vs low study design quality, revealed no differences. The reviewers concluded that the existing evidence did not provide support for heliox administration to patients presenting to the ED with moderate-to-severe acute asthma.[5]

Chest recently published 2 systematic reviews of heliox therapy in acute asthma.[6,7] These reviews and their accompanying editorials[8,9] illustrate how the message from the same basic data can be spun differently by different authors.

Rodrigo et al[6] reviewed both randomized and nonrandomized prospective controlled trials comparing heliox to placebo, with results including pulmonary function tests and other physiologic measures, adverse effects, hospital admissions, and clinical outcomes. They included 7 trials with a total of 392 patients. Either PEF or FEV_1 was the primary outcome variable in 6 studies; 2 studies measured airway resistance. Pooling the data from all studies, there were no differences in these outcomes with heliox vs placebo. Data from those studies that used heliox to deliver nebulized therapy (including the study by Kress et al summarized above[4]), found a nonsignificant overall increase in pulmonary function (standardized mean difference -0.21; 95% confidence interval, -0.43 to 0.01), and no difference in the rate of hospital admission. Two of these latter studies that used heliox-driven nebulization found significant increases in heart rate, but no clinically important side effects were reported. Rodrigo et al concluded that, although the existing studies are small and suffer from various design weaknesses, available evidence does not support the administration of heliox to ED patients with moderate-to-severe asthma.

In an editorial accompanying the Rodrigo review, Manthous[8] points out that no study to date has examined the really important issue of whether heliox improves outcomes in patients with acute severe asthma who do not respond satisfactorily to other therapies in the ED. He cautions that heliox should not be used routinely, but that it would be reasonable to try it in patients with severe, refractory status asthmaticus—if used carefully, as he and others have described.[2] Manthous also mentions that, in his last 10 years of practice, he has not encountered a case of severe asthma that did not respond to aggressive management (without heliox).

In a different take on the same basic data set and in the same issue of *Chest*, Ho and associates[7] reported an extensive statistical examination of pooled data from 4 of the 7 studies (278 patients) reviewed by Rodrigo et al. Using data from these 4 studies, Ho et al performed meta-analyses on PEF as a percent of the predicted value, saturation as measured by pulse oximetry, and dyspnea index. "These meta-analyses demonstrated an advantage with the use of heliox when compared with airO_2 at the 92% [*sic*] confidence level for PEF."[7] The weighted mean difference to which Ho et al refer was +3%, with a 95% confidence interval of -2% to +8%. Similarly, they describe a "slight improvement" in dyspnea index with heliox vs air-oxygen, with a 95% confidence interval of 0.04 to 1.16. No differences were claimed for pulse oximetry. Ho et al conclude that heliox may offer "mild-to-moderate benefits" in patients with acute asthma within the first hour of use, but less apparent benefit subsequently. Ho et al cite air entrainment around the mask (and thus dilution of the helium) as a methodologic flaw in the studies that did not show heliox to be superior to air-oxygen mixtures, and also discuss other possible reasons why other reviews have not found statistically significant benefits from heliox therapy.

Kass, in an editorial accompanying the Ho et al review[9], describes 2 patients with severe acute asthma who improved dramatically on heliox, but cautions that patients should be carefully selected for treatment with this agent. He points out that, since heliox is not therapeutic in itself but only a bridge until the primary agents exert their effect, ". . . it is unlikely that it will reduce

hospital admissions, hospital or ICU length of stay, or hospital mortality. It will provide rapid and marked relief of dyspnea to many patients without any detrimental effects. Since its therapeutic index is so high and its onset and offset of action are so rapid, it may find a useful niche in the prehospital setting when used by emergency medical technicians and possibly by an occasional labile asthmatic patient at home."[9]

What is the Downside?

As mentioned, helium is inert, and heliox has no inherent adverse effects. However, its effect on gas density, and hence its potential physiologic effects, wane rapidly as FIO_2 rises, and it is doubtful whether patients requiring much more than 30% oxygen could be expected to benefit. It would not be appropriate to allow a patient to remain hypoxemic in order to administer heliox. Hypoxemia is potentially life-threatening in acute asthma, and its correction is much more important than any potential gain from the use of heliox.

Heliox may adversely affect the function of respiratory care equipment such as flow meters, ventilators, nebulizers, and pulmonary function monitors.[10,11] However, in my opinion, the most important potential "adverse effect" of heliox in patients with acute severe asthma would be if its use delayed or de-emphasized the most effective therapies for this condition—aerosolized bronchodilators and systemically administered corticosteroids.

What is the Bottom Line?

Heliox has become a recognized therapy in acute asthma, and it is within the scope of accepted practice to try it in patients whose asthma is severe and who do not respond to intensive initial interventions. Its use would seem to make the most sense in patients with very severe acute asthma of sudden onset, as these patients may represent a subset of asthmatics at increased risk of death.[12,13] However, my opinion is that it is better to use proven therapies more aggressively than to add less established and more controversial interventions such as heliox—particularly if "the basics" have not been given using optimal technique, in sufficient doses, and for a long enough time.

As with other adjunctive therapies in acute respiratory failure (inhaled nitric oxide comes to mind), compelling physiologic rationale and anecdotal successes do not necessarily translate to clinically important benefits for patients on more rigorous examination using the scientific method. In acute severe asthma, prompt, aggressive therapy with aerosolized bronchodilators and systemic corticosteroids results in marked improvement over several hours in the vast majority of patients. Despite its safety and relatively modest cost, the evidence for a clinically important additional benefit of heliox in this setting is not convincing. ■

References

1. Barach AL. The use of helium in the treatment of asthma and obstructive lesions of the larynx and trachea. *Ann Intern Med*. 1935;9:739-765.
2. Manthous C, et al. Heliox in the treatment of airflow obstruction: A critical review of the literature. *Respir Care*. 1997;42:1034-1042.
3. Hess DR, et al. The effect of heliox on nebulizer function using a beta-agonist bronchodilator. *Chest*. 1999;115(1):184-189.
4. Kress JP, et al. The utility of albuterol nebulized with heliox during acute asthma exacerbations. *Am J Respir Crit Care Med*. 2002;165(9):1317-1321.
5. Rodrigo G, et al. Heliox for treatment of exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2002;(2):CD003571.
6. Rodrigo GJ, et al. Use of helium-oxygen mixtures in the treatment of acute asthma. *Chest*. 2003;123:891-896.
7. Ho AMH, et al. Heliox vs air-oxygen mixtures for the treatment of patients with acute asthma. *Chest*. 2003; 123:882-890.
8. Manthous CA. Heliox for status asthmaticus? *Chest*. 2003;123:676-677.
9. Kass JE. Heliox redux. *Chest*. 2003;123:673-676.
10. Chatmongkolchart S, et al. In vitro evaluation of aerosol bronchodilator delivery during noninvasive positive pressure ventilation: Effect of ventilator settings and nebulizer position. *Crit Care Med*. 2002; 30(11):2515-2519.
11. Chatmongkolchart S, et al. Heliox delivery with noninvasive positive pressure ventilation: A laboratory study. *Respir Care*. 2001;46(3):248-254.
12. Wasserfallen JB, et al. Sudden asphyxic asthma: A distinct entity? *Am Rev Respir Dis*. 1990;142(1):108-111.
13. Woodruff PG, et al. Sudden-onset severe acute asthma: Clinical features and response to therapy. *Acad Emerg Med*. 1998;5(7):695-701.

CME / CE Questions

5. In patients with ARDS who were treated with inhaled nitric oxide and high frequency oscillatory ventilation:

a. survival was significantly improved compared to conventional ventilation.

b. cardiac output increased with the initiation of inhaled nitric oxide.

c. the duration of mechanical ventilation was significantly improved compared to conventional ventilation.
d. there was an increase in PaO_2/FIO_2 ratio of at least 20% in the majority of patients.
e. None of the above

6. When patients with severe ARDS were switched from conventional to high-frequency oscillatory ventilation:
a. 28-day survival increased from 20% to 33%.
b. PaO_2/FIO_2 ratio increased by > 20% in 83% of the patients.
c. the incidence of barotrauma decreased by 25%.
d. mean airway pressure could be reduced by 25%.
e. None of the above

7. How many patients with ICU stays of at least 3 days would need to receive weekly doses of human recombinant erythropoietin in order to prevent 1 patient from receiving a unit or red blood cell transfusion?
a. 3
b. 7
c. 10
d. 15
e. 22

8. Administration of erythropoietin (40,000 U each week) to ICU patients resulted in which of the following?
a. A statistically significant reduction in ICU length of stay
b. A statistically significant reduction in 28-day mortality
c. A statistically significant reduction in red blood cell transfusions
d. All of the above
e. None of the above

9. Heliox may benefit patients with acute severe asthma by:
a. decreasing the work of breathing.
b. decreasing hyperinflation.
c. improving aerosol deposition.
d. All of the above
e. None of the above

10. Available evidence indicates that heliox in acute asthma:
a. improves arterial oxygenation.
b. decreases the need for endotracheal intubation.
c. decreases ICU and hospital length of stay.
d. All of the above
e. None of the above

11. Heliox:
a. is less dense than air.
b. is less viscous than air.
c. is both less dense and less viscous than air.
d. inactivates beta-agonist bronchodilators.
e. cannot be used during mechanical ventilation.

Answers: 5. (d); 6. (e); 7. (c); 8. (c); 9 (d); 10. (e); 11. (a)

Readers are Invited. . .

Readers are invited to submit questions or comments on material seen in or relevant to *Critical Care Alert*. Send your questions to: Robin Mason, *Critical Care Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. For subscription information, you can reach the editors and customer service personnel for *Critical Care Alert* via the internet by sending e-mail to robin.mason@ahcpub.com. ■

CME / CE Objectives

After reading each issue of *Critical Care Alert*, readers will be able to do the following:

- Identify the particular clinical, legal, or scientific issues related to critical care.
- Describe how those issues affect nurses, health care workers, hospitals, or the health care industry in general.
- Cite solutions to the problems associated with those issues.

In Future Issues:

Practice Guidelines Reduce Unnecessary Testing in the CCU

CRITICAL CARE Plus

EXPANDING YOUR FOCUS IN INTENSIVE CARE

Doing More With Less: The Advantages of an 'E-ICU'

Intensivist-designed system making inroads

By Julie Crawshaw

NATIONALLY, IT'S ESTIMATED THAT PATIENTS NEED THE SERVICES OF 30,000 INTENSIVISTS. SINCE ONLY ABOUT 6,000 board-certified intensivists are available, there's a big gap to be filled, and one company offering online clinical services has started filling it.

Begun in 1998 by Brian Rosenfeld, MD, and Michael Breslow, MD, former intensivists at Johns Hopkins Hospital, VISICU, Inc. in Baltimore, offers an online comprehensive clinical services program that the company says enables healthcare organizations to save lives, improve outcomes, and reduce costs. The company's Continuous Expert Care Network (CXCN) recently became the first commercialized offering to meet patient care safety standards set by the Leapfrog Group, a consortium of Fortune 500 companies and other large private and public healthcare purchasers organized to reward hospitals for higher standards for patient safety.

About 500,000 patients die every year in U.S. ICUs, according to Leapfrog's physician staffing report. The group's recently announced ICU patient safety standards call for full-time staffing by certified intensivists as a way to save more than 50,000 patient lives annually, nationwide. Rosenfeld's and Breslow's initial e-ICU research showed huge reductions in risk-adjusted mortality, length of stay and costs.

Sentara Healthcare, a Norfolk, Virginia-based not-for-profit health care organization that serves Southeastern Virginia and Northeastern North Carolina, began using CXCN on its patients in June 2000 after a year of preliminary work. In its first year of using CXCN, Sentara says it accomplished a 26% reduction in severity-adjusted ICU mortality, a 23% in severity-adjusted hospital mortality for those ICU patients and reduced ICU length-of-stay by about 17%.

"We've found that the magnitude of change has been maintained through time discharge," says Gene Burke, MD, Sentara's medical director for its e-ICU.

Sentara's six-hospital system, which serves a community of one and a half million residents, has fewer than 20 board-certified medical intensivists and a handful of surgical intensivists, to serve its 150 ICU beds. "We obviously have a huge need," Burke says, Sentara launched CXCN in a 10-bed, tertiary medical-surgical ICU, followed by an eight-bed, tertiary vascular post-operative ICU and two 16-bed community hospitals with combined CCU/ICUs.

Long-Distance Monitoring

CXCN's technology works from a remote e-ICU site outfitted with a VISICU network and database. Clinicians use the CXCN's telemedicine technology and smart alarms to monitor and manage ICU patients. There are three parts to VISICU's program: telemedicine, outcomes analysis and decision support.

The telemedicine, real-time audio-video communication with the bedside and nursing station are monitored

through secure landlines into an electronic ICU. One eICU computer screen contains the patient's medical records, another acts as a slave to a monitor at the patient's bedside, and one serves as audio-video communication in the patient's room. "I can do a pupillary exam on the patient even though I'm 20 miles away," Burke says. "I can be wired to 50 ICU beds, nowhere near a hospital."

Burke refers to a fourth monitor as smart alarms, a collection of software programs designed to look at constant, real-time monitoring of vital signs. "If a patient has a significant drop in pulse-oximetry saturations, either an absolute level or a trend from what has been the baseline, the software automatically alerts me and draws my attention to that patient."

The system has similar alarms for heart rates, both for absolute and trends. Other alarms, including one for a small-magnitude drop in blood pressure accompanied by an increased pulse rate and another for creatinine-level changes, are under construction.

CXCN is based on an electronic medical record proprietary to VISICU constructed for critical care units. It has a variety of screens that allows users to see summaries of patient data broken down by organ systems. All laboratory, X-ray and trend analyses remain available on the system, allowing retrospective data analysis to help determine clinical change, a capability Burke points out is not available at the bedside.

"Looking at the monitor in a hospital room, you see only about the last 10 seconds, and that's it." Burke says. "And once it's off the screen you can't call it back."

CXCN, Burke says, can store months' worth of data, useful for trend analysis. The system also keeps the intensivist physician in communication with other physicians, nurses, respiratory therapists, nutritionists and pharmacists who are at the bedside.

Better Outcomes Analysis

The complexity of the medical database is so great, Burke says, that most hospital systems have not put a lot of money into software tools for analyzing clinical outcomes. "It's a rare hospital with a system the physician can ask to show how much resource is being consumed for care of an ICU patient with a given diagnosis," Burke says. "Most systems can't tell you your cost-of-care or complication rate, yet we need those data to understand where we do things well and where we need to do better."

Burke says CXCN uses APACHE III software, a predictive tool for critical care that allows assessing a collection of patient problems to ascertain the most probable outcomes. "We look at our performance compared to that prediction, try to find places where our performance is not what it could or should be," Burke says. "That's a huge assist."

Burke says that through using CXCN, Sentara has found opportunities for shortening length of stay and significant financial savings. "We are trying to bring evidence-based medicine to the critical care environment," Burke says. "About 92,000 people per year die of avoidable medical complications."

Decision-Support Tool

The Source is VISICU's proprietary name for the third component of its system, a collection of algorithms and suggested guidelines for frequently occurring critical care problems.

Asking five physicians about a problem will likely result in at least three different answers, Burke says, noting that variability decreases outcomes and increases costs. To counter this, VISICU hired a collection of experts in various organ disciplines and asked them to write succinct literature-based guidelines.

"I have a collection of algorithms available to me in this computer," Burke says. "I enter specific patient data and the program walks me through the decision process, helping me come to the best practice."

Burke also uses the Source as a teaching tool for Sentara's interns and residents, who can use its bibliography to access articles via the Internet. Thus a resident encountering a problem with a patient in the middle of the night can do a quick read with a selective bibliography and show up for rounds on the following morning with an article pertinent to that problem. "It really facilitates graduate education," Burke says.

(For more information contact Gene H. Burke at [757] 461-0241, or Cheryl Isen at VISICU, [425] 222-0779.) ■

A La Carte Approach to Critical Care Works Well

Moving the monitor instead of the patient

NINE YEARS AGO, MUHLENBERG REGIONAL MEDICAL Center in Plainfield, NJ, opened Progressive Care, an intermediate critical care floor to serve patients with diagnoses and conditions that qualify them for ICU care

but who don't require the full, intensive nursing and monitoring that an ICU traditionally provides. The system has worked so well that the facility has added a second such flexible unit.

The idea for creating a flex-unit to relieve pressure on the center's ICU first occurred to Eva Besserman, DO, Director of Critical Care during one especially busy triage. Besserman noticed that patient transfers to or from the ICU depended as much on which nursing environment could fill the patient's needs as it did on the condition of the patient. That insight led to combining a medical-surgical and an intermediate care unit. "We decided to move the monitor instead of moving the patient from bed to bed," Besserman says.

Besserman says everyone at Muhlenberg bought into the flex unit approach during a time of gridlock when the facility had no place to put a chronic vent patient. "The patient had a transfer order but no med-surg beds were available," Besserman says. "We grabbed a monitor from another unit and the critical care nurses were able to treat this patient much more quickly than they could have if we'd had to transfer her to another unit. She was treated within moments, and that locked it in."

That patient had been hospitalized for about four months, and from that moment on she was never moved. The idea that began as a way to further a resource turned into a success story that created a facility-wide buy-in. "It wasn't just me talking about how a flex-unit would be worthwhile," Besserman says. "Everyone saw it for themselves."

Better Outcomes

Muhlenberg's flex-unit reduces demands on both the ICU and emergency rooms by taking patient overflow, thus creating an alternative model for patient care based solely on patient needs, says Sheri Cleaves, RN, MSN, CCRN, clinical nurse specialist at Muhlenberg. Cleaves says the flexible approach has raised nurses' levels of job satisfaction and improved patient outcomes as well. "There's a very big focus on performance improvement in these units," she says. "And in the last year, we've been able to stabilize the nursing staff on that unit, who now report a very high level of job satisfaction."

Improved outcomes were duly noted during Muhlenberg's last Joint Commission survey. Figures showed the flex-unit had reduced its central line infection rate from around 6% to 1.9% and dropped the incidence of ventilator-related pneumonias from 12% to 5%.

Cleaves attributes much of the improved nursing morale to the fact that, under the flexible system, nurses are able to keep the same patients for the entire time that those patients are in the hospital. "It's good because you're not just taking care of a patient for a couple of days and transferring them off the floor before starting all over again with a new patient," Cleaves observes. "When a physician wants a patient who does not need full ICU level care to receive critical care monitoring, the patient gets that through our a la carte approach."

Admission Criteria the Same

Muhlenberg's flex-unit is for patients who don't need critical care but who do need a more intensive nursing than a regular floor patient. Cleaves notes that the criteria for admission haven't changed since the unit's inception. Patients with acute but reversible diseases receive priority over cases with prognoses of chronic, irreversible or terminal and leaves complicated ventilator patients and those who are hemodynamically unstable for the ICU. Neither does the flex-unit take cases with complicated intraoperative tracheotomies, patients who require A-line Swan Ganz monitoring, continuous arterial venous hemofiltration, continuous arterial venous hemofiltration dialysis or balloon pumps.

Other criteria include:

- Cardiac patients with rapidly-changing monitoring needs and levels of nursing care who may benefit from a flexible monitoring unit;
- Patients who require continuous pulse oximetry with or without cardiac telemetry monitoring;
- Medical-surgical patients who need frequent vital-signs monitoring and intensive nursing care with or without cardiac monitoring, e.g. gastrointestinal bleeding, asthma, sepsis and hypertensive conditions;
- Patients with uncomplicated bilevel airway pressure who don't require one-on-one nursing or titration of sedative drips;
- Cases in need of insulin drips with fingertip glucose every two hours, in addition to uncomplicated illnesses;
- Newly intubated or tracheotomy ventilator patients who don't require titratable drips or sedatives under long or short-term management;
- Major post-surgery cases in need of close observation.

Trained for Critical Care

Because all flex-unit nursing staff members are trained for critical care, Cleaves notes that there is great consistency of care throughout all shifts.

"Through active recruitment, we've been able to get the right people there, people who are interested in investing themselves in that kind of unit," Cleaves says, adding that the unit now has assistant nurse managers on both the day and night shifts. "It's one of our most stable units for staffing and outcomes. Staff work as a multidisciplinary team, with respiratory, dietary, social worker, and case manager giving our nurses support."

In 1999, Muhlenberg installed new monitoring systems. The same tech team now monitors patients in coronary care, intermediate care and med-surg, and can quickly notify appropriate personnel if there are problems.

One weekend while the facility's IMCU was very busy while the CCU wasn't busy at all, Besserman realized she could further enhance flexibility by removing the wall that divided the two units. When the facility's coronary care unit was remodeled, the wall came down, creating one unit with the capacity to take care of patients on both sides.

Besserman says that some division of patients remains, but when an IMCU patient needs a higher level of care, nurses who already know the patient are there to give it. "Now we can use all the beds without restricting bed capacity for either unit," Besserman notes. "It's really reduced the logjam we used to have in critical care."

The appropriate level of care for the wide case mix of patients admitted the Flex Unit is identified by color coding patients' names on the unit's nursing assignment board.

Level I: Red denotes extremely ill patients who need some ICU-level care such as:

- Vital signs every four hours;
- Cardiac monitoring as needed;
- Charting or critical care flow sheet;
- Ventilator support with telemetry;
- High-risk status requiring frequent assessment.

Level II: Green denotes non-telemetry cases that require frequent nursing assessment

- Vital signs every 4 hours;
- Charting on critical care flow sheet;
- Ventilator patient (non-telemetry) with vital signs;
- Charting every 4 hours;
- Telemetry discontinued by close observation.

Level III: Blue denotes nontelemetry cases that require medical-surgical care:

- Vital signs every eight hours;
- Charting on medical-surgical flow sheet.

(For more information contact Eva Besserman or Sheri Cleaves at [908] 668-2000.) ■