Heliox for children with acute asthma: Has the sun set on this therapy?

Helium is the second most plentiful element in the universe and the lowest density of any gas except hydrogen. It is also biologically inert and nonflammable, making it useful for a variety of industrial, scientific, and medical indications, including the cooling of superconducting magnets (such as those used in magnetic resonance imaging), protection against nitrogen narcosis in deep sea diving, and providing lift for blimps and balloons (1). Helium was first discovered while studying the spectrum of the solar corona during an eclipse in 1868. It was reproduced on earth in 1895 in experiments by chemist William Ramsay. The name, “helium,” from the Greek “Helios” alludes to its solar “origins.”

When used medically, helium is delivered in a mixture containing between 20% and 40% oxygen (heliox) to replicate the nitrogen-oxygen content in air. Due to its lower density than air, heliox flows more efficiently with less turbulence and resistance through small or obstructed airways. The potential benefits of this therapy to treat asthma were first described by Alvan Barach in 1934; however, heliox was not widely used until much later (2, 3). In the 1980s, with increasing rates of asthma-related hospitalization and death, there was renewed interest in this therapy in children who were refractory to conventional therapies for acute asthma (4–7).

Recently, the incidence of asthma-related hospitalizations and deaths has plateaued, but severe refractory asthma exacerbations, or status asthmaticus, remains a significant problem, affecting an estimated 10,000 children each year in the United States. Treatment for status asthmaticus is typically subjective and based on provider preference with little evidence-based medicine and wide variation in the treatments by region, by hospital, and by provider (8, 9). Large-scale studies are challenging to conduct in children with acute asthma for a variety of reasons, including the relatively short durations, difficulties in obtaining reliable surrogate end points in this population, and difficulties recruiting critically ill children for clinical trails.

Heliox is a particularly attractive therapy in children with acute asthma, in whom age and size-related differences in airway diameter can lead to more turbulent airflow than in adults with larger airways. Heliox, therefore, might be more likely in this population to convert density-dependent turbulent airflow to a more laminar flow and thereby reduce airway resistance and improve work of breathing. However, to significantly lower the density of the inhaled gas, helium needs to comprise 60% to 80% of the mixture, limiting the usefulness of heliox in significantly hypoxemic children with status asthmaticus.

There have been four previous, randomized, placebo-controlled studies examining heliox for the treatment of acute asthma in children (4–7). In the first two studies by Carter et al and Kudukis et al, 15 mins of heliox therapy was provided to small groups of children (n = 11 and 18 patients, respectively) (4, 5). Contradictory findings were noted in these studies, with Kudukis et al finding improvement in clinical asthma score and pulse oximetry, whereas Carter et al found no improvements in pulmonary function testing or clinical asthma score (4, 5). However, the study by Carter et al was conducted in children who had been treated for at least 6 hrs in the hospital setting, whereas the study by Kudukis et al was conducted on children earlier in their disease process (4, 5). It is reasonable to theorize from these results that the benefits from heliox therapy might be found during the initial treatment period.

The next two randomized placebo-controlled studies were conducted in children with acute asthma in the Emergency Department setting (6, 7). These studies by Kim and Rivera, also included small numbers of patients (n = 30 and 41, respectively), and provided heliox for short durations (240 and 20 mins respectively). These studies had contradictory findings as well. The study by Kim et al (6), with the longer duration of heliox therapy showed improvement in clinical asthma score, whereas the study by Rivera et al (7) did not. It would be reasonable to theorize from this that a longer duration of heliox therapy might be beneficial.

In this issue of Pediatric Critical Care Medicine, the study by Bigham et al is the first to treat children with heliox-driven albuterol throughout the duration of their hospitalization (10). As such, this study might be expected to have the greatest potential to demonstrate benefit, and to best clarify when heliox might be beneficial in the natural history of acute asthma. Forty-two children with status asthmaticus were randomized to receive albuterol nebulizer treatments driven either by heliox or by a conventional air-oxygen mixture (10). Helium-driven albuterol would be expected to increase nebulized drug delivery, and improve gas exchange to the distal airways, thereby improving outcomes in these patients. However, as nicely illustrated in their Figure 1, there were no differences in the clinical asthma scores of the patients in either group throughout the duration of hospitalization (10). Nor were there differences in time to eligibility to hospital or intensive care unit discharge (10).

Bingham et al experienced some of the problems found in other studies of children with acute asthma. Recruitment was low, with only 42 enrolled—of the 310 children eligible for the study over a 20-month period. In addition, the authors needed to use a clinical asthma score as a
surrogate outcome measure and to quantify illness acuity. Although the reliability of this score at their institution was nicely documented, clinical asthma scores are inherently subjective. Finally, because the helium can adversely affect ventilator function (11), the authors were unable to include the most severely ill children in their study. If these ventilatory problems are corrected, it may be that children with impending respiratory failure would benefit from helium therapy.

So, is this the end of helium for the treatment of status asthmaticus in children? Probably not. Status asthmaticus is difficult to study in children and the four (now five) randomized controlled studies have included a total of only 124 patients. Given these relatively small numbers, there may be a population of children who will still benefit from this therapy. Even despite this well-designed and conducted study, when your back is against a wall, as it occasionally is in the intensive care unit, I suspect that there will still be a role for a trial of helium in select children with refractory status asthmaticus.

Christopher L. Carroll, MD, MS
Connecticut Children’s Medical Center
Hartford, CT

REFERENCES

1. Catlett RA: Helium, the wonder gas. The Scientific Monthly 1949; 69:222–228

What’s new in extracorporeal cardiopulmonary resuscitation?*

Extracorporeal cardiopulmonary resuscitation (E-CPR) use continues to increase as a rescue therapy for refractory in-hospital cardiac arrest in children (1). Like the adult population, survival with E-CPR has not increased with time (2). The survival rates (44% in children, 27% in adults) are sufficient to make E-CPR an accepted resuscitation option; however, refining patient selection criteria will facilitate judicious use of this resource-intensive therapy. In this issue of Pediatric Critical Care Medicine, the analysis of E-CPR in the pediatric population reported by Raymond et al (1) is from the National Registry of Cardiopulmonary Resuscitation database, which, in contrast to previous multicentered studies drawn from the Extracorporeal Life Support Organization database (3, 4), allows for evaluation of pre-extracorporeal membrane oxygenation (ECMO) resuscitation factors and assessment of immediate cognitive outcomes.

For children resuscitated with E-CPR, few arrest variables significantly impacted survival. There was no difference in survival of patients in pediatric vs. mixed hospitals, those already in an intensive care unit or operating room compared with other hospital areas, or related to time of day or weekday compared with weekend arrest. However, there was a trend for worse survival among children with E-CPR deployed on the weekend. Interestingly, neither the duration of cardiopulmonary resuscitation nor the prearrest presence of an arterial line impacted survival. Children with pre-existing renal insufficiency or electrolyte abnormalities had significantly worse survival.

Very little data about the population of patients who never achieve return of spontaneous circulation are published, but this group accounts for 48% pediatric patients with in-hospital cardiac arrest (5). The group selected for E-CPR is likely different from both the overall population of children requiring cardiopulmonary resuscitation and those who do not achieve return of spontaneous circulation but are not placed on ECMO. E-CPR is used in children who are similar to the patients most likely to achieve return of spontaneous circulation with traditional in-hospital cardiopulmonary resuscitation (6, 7); in general, they are infants with cardiac disease whose cardiac arrests occurred in pediatric intensive care units during working hours and their presenting rhythm at the time of arrest is either ventricular fibrillation or pulseless ventricular tachycardia. These factors can assist the clinician in making timely decisions regarding use of E-CPR. A recent pediatric intensive care unit study (8) reported no survival among children when the arrest was >13 mins without ECMO. Thus, decisions to activate ECMO should be made rapidly. The same study described improved survival in patients

*See also p. 362.

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For information regarding this article, E-mail: Susan.Bratton@hsc.utah.edu

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