Emergency Extracorporeal Life Support for Asphyxic Status Asthmaticus

Mark E Mikkelsen MD, Meredith E Pugh MD, John H Hansen-Flaschen MD, Y Joseph Woo MD, and Jeffrey S Sager MD

We report a case of successful use of extracorporeal life support (ECLS) as salvage treatment in an adult with acute, severe, reversible respiratory failure due to asphyxic status asthmaticus. Conventional measures were ineffective to combat the dynamic hyperinflation; the patient had intrinsic positive end-expiratory pressure > 30 cm H_2O. We initiated emergency ECLS at the bedside, and after 55 hours of ECLS his respiratory mechanics had markedly improved and he was subsequently weaned off of ECLS and decannulated, without vascular, pulmonary, or neurologic complications. This article reviews the history of ECLS for adult respiratory failure and its application for life-threatening status asthmaticus. This case illustrates the effective use of ECLS for acute respiratory failure due to asphyxic status asthmaticus, and to our knowledge is the first reported case in which the patient's impending cardiopulmonary arrest was due to an unsustainable level of intrinsic positive end-expiratory pressure. *Key words: extracorporeal life support, status asthmaticus, mechanical ventilation, intrinsic positive end-expiratory pressure, PEEP, dynamic hyperinflation*. [Respir Care 2007;52(11):1525–1529. © 2007 Daedalus Enterprises]

Introduction

Extracorporeal life support (ECLS) is the use of a modified heart-lung machine at the bedside in the intensive care unit for days or weeks to provide support of gas exchange and perfusion so as to permit recovery during severe acute cardiopulmonary failure, while avoiding ventilator-induced lung injury. Though no randomized study has demonstrated a significant mortality reduction in adults with acute respiratory failure treated with ECLS as compared to conventional therapy, the potential mortality benefit of ECLS in the treatment of acute, severe, reversible respiratory failure exists. In the United States, severe asthma exacerbations result in approximately 400,000 hospitalizations annually.[1] Status asthmaticus, a disease with an estimated mortality of 6.9% when mechanical ventilation is required, exemplifies a disease in which prompt, appropriate utilization of ECLS could save lives.[2]

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Case Summary

A 33-year-old Indonesian male presented to the emergency department complaining of crescendo dyspnea over 24 hours, refractory to inhaled albuterol. He had a history of asthma since childhood and had 2 prior intubations for severe asthma. Approximately 6 weeks prior to admission he developed cough, dyspnea, and wheezing. As an outpatient he was given an albuterol metered-dose inhaler and

Mark E Mikkelsen MD, Meredith E Pugh MD, John Hansen-Flaschen MD, and Jeffrey S Sager MD are affiliated with the Division of Pulmonary, Allergy, and Critical Care; and Y Joseph Woo MD is affiliated with the Division of Cardiothoracic Surgery, University of Pennsylvania Health System, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania.

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Correspondence: Mark E Mikkelsen MD, Pulmonary, Allergy, and Critical Care Division, Hospital of the University of Pennsylvania, 836 W Gates Pavilion, 3400 Spruce Street, Philadelphia PA 19104. E-mail: mark.mikkelsen@uphs.upenn.edu.

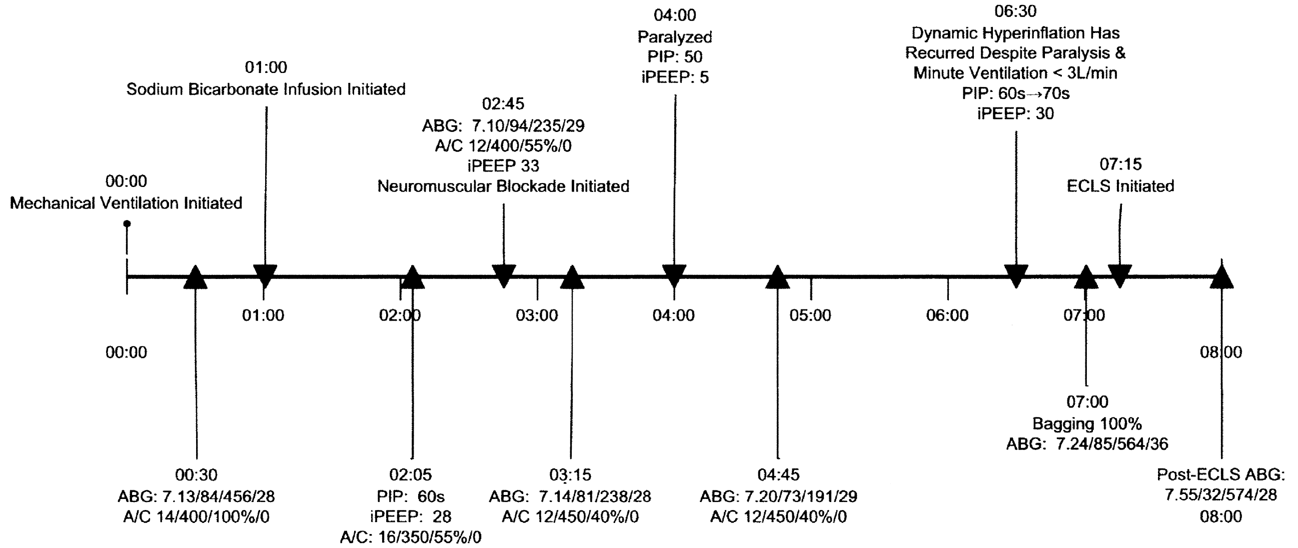

Fig. 1. Timeline of events from initiation of mechanical ventilation to initiation of extracorporeal life support (ECLS). The arterial blood gas (ABG) values shown are pH, P_{aCO_2}, P_{aO_2}, and serum bicarbonate. The assist-control (A/C) ventilation parameters are respiratory rate, tidal volume, fraction of inspired oxygen, and positive end-expiratory pressure. PIP = peak inspiratory pressure. iPEEP = intrinsic positive end-expiratory pressure.

escalating doses of oral prednisone, with no subsequent improvement in symptoms.

In the emergency department he was treated with intravenous methylprednisolone, magnesium sulfate, inhaled bronchodilators, and supplemental oxygen. He was admitted for observation and on hospital day 2, despite intravenous corticosteroids and frequent nebulized bronchodilators, he developed asphyxic status asthmaticus that required emergency intubation and mechanical ventilation.

Bouts of profound bronchospasm occurred episodically, with hypercapnia and acidosis, despite repetitive inhalation of albuterol and intravenous corticosteroids, deep sedation with intravenous fentanyl and lorazepam, intermittent subcutaneous epinephrine, and sodium bicarbonate infusion. Approximately 2 hours after initial intubation the peak inspiratory pressure increased to > 60 cm H_2O and plateau pressure and intrinsic positive end-expiratory pressure (PEEP) was in excess of 30 cm H_2O.

Figure 1 shows the timeline of events, including arterial blood gas measurements and ventilator settings. Attempts to minimize the patient's dynamic hyperinflation by prolonging the expiratory time, initially by decreasing the respiratory rate, were minimally effective in decreasing the high peak airway pressure and high static pressure. Attempts to further prolong the expiratory time with higher inspiratory flow (as high as 80 L/min) were limited by even higher peak airway pressure. After a bolus and subsequent infusion of vecuronium, the peak inspiratory pressure decreased to 50 cm H_2O, plateau pressure decreased to 15 cm H_2O, and intrinsic PEEP decreased to 5 cm H_2O. Arterial blood gas values prior to paralysis were pH 7.10, P_{aCO_2} 94 mm Hg, and P_{aO_2} 235 mm Hg. Cardiothoracic surgery was consulted for consideration of ECLS in the event that his condition deteriorated.

Despite adequate sedation and paralysis, airflow obstruction and dynamic hyperinflation worsened. Portable chest radiographs, obtained through the course of the evening, demonstrated neither atelectasis nor infiltrates or other abnormality. Two hours after the initiation of paralytics, the patient was placed on a continuous infusion of cisatracurium, titrated by critical care nursing, via peripheral nerve stimulator, and was administered subcutaneous epinephrine, without effect. Whether the improvement observed in respiratory status after initial administration of neuromuscular blockade reflected the lability of the patient's acute respiratory failure, or rather coincided with the transition where his obstruction progressed to a more severe form is unknown. Over the next 3 hours, having minimized the contribution from the patient's own respiratory musculature, the patient's airflow obstruction progressed to the degree that his intrinsic PEEP again approached 30 cm H_2O, with peak airway pressure > 75 cm H_2O despite respiratory minute ventilation set at < 3 L/min (the tidal volume was decreased sequentially from 450 mL to a nadir of 200 mL, with a respiratory rate as low as 10 breaths/min). Eventually, due to high-pressure limits, he was receiving tidal volume of < 50 mL with any ventilation mode.

This untenable respiratory status, in the presence of relative hypotension that developed over the preceding hours, despite aggressive volume resuscitation, prompted emergency initiation of venovenous ECLS to counteract the patient's severe dynamic hyperinflation and impending cardiopulmonary arrest. Venovenous bypass was established at the bedside via insertion of a 16 French venous cannula into the right internal jugular vein and a 22 French Heartport long venous cannula into the right common femoral vein and positioned into the inferior vena cava-atrial junction, with the percutaneous Seldinger technique. The cannulas were connected to the ECLS circuit, and ECLS flow was initiated with femoro-atrial flow at 3.5 L/min, given evidence that this diminishes recirculation.[3] Twenty minutes after initiating ECLS, the patient became transiently hypotensive, which required administration of phenylephrine. Vasopressor support was quickly weaned off over the next several hours.

Arterial blood gas values rapidly normalized on ECLS, and a lung-protective ventilation strategy with pressure-control ventilation was employed to minimize barotrauma. On hospital day 3 he experienced right-lung atelectasis with hypoxemia secondary to mucus plugging, which was treated with therapeutic suctioning via bronchoscope. While on ECLS he developed acute renal failure, which resolved without hemodialysis. In addition, he remained sedated and paralyzed and continued to receive methylprednisolone.

His respiratory mechanics improved over the next 48 hours, and he was subsequently weaned off ECLS 55 hours after initiation and decannulated without vascular or pulmonary complications 1 day later. On hospital day 10, he was successfully extubated and had normal mentation. On hospital day 12 he was transferred out of the intensive care unit. He was discharged home after 21 days in the hospital.

Discussion

The first successful use of cardiopulmonary bypass at the bedside was reported by Hill and colleagues in 1972, in a 24-year-old male who developed posttraumatic acute respiratory distress syndrome (ARDS).[4] Though case reports in the 1970s bolstered the use of ECLS for acute cardiopulmonary failure, the early trial termination for lack of efficacy in an National Institutes of Health-sponsored multicenter prospective randomized investigation of acute respiratory failure marked a major setback in the evolution of ECLS.[5] As a result of the National Institutes of Health trial, published in 1979, ECLS was used primarily in neonatal centers in the 1980s.

Advances in technology and favorable outcomes in neonatal centers prompted investigators to apply ECLS to adults again in the late 1980s. In 1986, Gattinoni and colleagues demonstrated that use of extracorporeal carbon dioxide removal in patients with ARDS was safe and associated with a survival advantage, when compared to historical controls.[6] However, a second randomized controlled trial, published in 1994, failed to demonstrate a survival advantage when extracorporeal CO_2 removal was used in addition to conventional mechanical ventilation in patients with severe ARDS,[7] which marked a second setback for ECLS in adult respiratory failure.

In 2000 Bartlett and colleagues published their experience of 1,000 ECLS patients at the University of Michigan, which was the largest series in one institution in the world.[8] Since 1990, 146 adult patients with respiratory failure have been treated at the University of Michigan. The etiology of respiratory failure in the 146 adults was either pneumonia or ARDS.

After searching for relevant English-language publications in MEDLINE from 1966 to September 2006, we discovered 2 prior case reports that described ECLS for adult asphyxic status asthmaticus in the United States,[9,10] and several case reports[11–14] and one small case series[15] from other countries. The indications given for utilizing ECLS in the case reports included cardiovascular compromise and/or cardiac arrest, which required veno-arterial ECLS,[9,11,13] and severe hypercapnic acidosis.[10,12,14] The indications for ECLS in the 3 patients in the case series included impending asphyxia demonstrated by severe, refractory hypercapnia and acidosis, hypoxemia and eventual shock, and dynamic hyperinflation demonstrated by subcutaneous emphysema and peak inspiratory pressure up to 50–60 cm H_2O.

In their case series, Kukita and colleagues[15] provided an algorithmic approach to mechanical ventilation in patients with status asthmaticus, which suggests that clinicians consider ECLS if, despite institution of hypoventilation and while tolerating increased peak inspiratory pressure, $pH < 7.2$, $P_{aCO_2} > 100$ mm Hg, or life-threatening conditions due to hypoxemia, hypotension, or barotrauma develop. Serial measurements of static pressures (plateau and intrinsic PEEP), in addition to peak inspiratory pressure, are not included in that algorithmic approach to mechanical ventilation in patients with status asthmaticus.

In addition, early, appropriate cardiothoracic surgery involvement is not included in the algorithm. Recent evidence suggests that mortality in patients who require ECLS may be directly related to the patient's cardiovascular stability and indirectly to whether the ECLS team has sufficient time to mobilize.[16,17] As such, early coordination between medical intensivists and cardiothoracic surgeons and trained support staff of established ECLS programs or transport to such a program must be prioritized to optimize the utility of ECLS in the care of the patient with acute, severe, reversible respiratory failure who is failing conventional therapy.

Once mechanical ventilation is required, alveolar hypoventilation is the guiding principle employed to combat the dynamic hyperinflation, and the resultant barotrauma and cardiovascular compromise, which characterizes status asthmaticus.[18] The safety limit of alveolar hypoventilation, however, is not known. Though Molfino et al observed severe hypercapnia (mean P_{aCO_2} 97.1 ± 31 mm Hg) and acidosis (mean pH 7.01 ± 0.11) in asthmatics experiencing respiratory arrest, those observations were made prior to initiating mechanical ventilation.[19] In contrast, other studies have found that, once mechanical ventilation is initiated, permissive hypercapnia is well tolerated up to P_{aCO_2} of 120 mm Hg.[20–22] As such, hypercapnic acidosis alone, the most-often-cited indication for ECLS in the aforementioned case reports, should rarely require ECLS.

The Extracorporeal Life Support Organization registry, which comprises 120 centers worldwide, reported in 2005 that nearly 29,000 patients have been treated with ECLS since its inception in 1989, including 972 adults for respiratory failure.[23] The most prevalent indication for ECLS in this population was ARDS, followed by bacterial pneumonia, viral pneumonia, and aspiration. Survival of the cohort of patients is dependent upon diagnosis, ranging from 49% (for "other" diagnosis) to 62% for viral pneumonia. Overall, survival was 54%. Nearly one third of the patients had other, unspecified indications for respiratory failure that required ECLS.

The Extracorporeal Life Support Organization registry includes 24 adults who are distinct from the patients in the aforementioned reports and series, who were treated with ECLS for respiratory failure due to refractory status asthmaticus.[24] Six patients were reported to the registry before 1995: 11 from 1996 to 2000, and 7 from 2001 to September, 2006. Sixty-seven percent of the patients were male. The mean age of these patients was 31.3 years (95% confidence interval 26.09–36.49 y) and the median duration of ECLS was 111.92 hours (95% confidence interval 71.19–152.64 h). 83.3% of the 24 patients survived to hospital discharge. After adjusting for age, severity of lung injury (ratio of P_{aO_2} to fraction of inspired oxygen), and duration of ECLS, ECLS in adult respiratory failure secondary to status asthmaticus is associated with greater survival than ECLS use for all other indications.[25]

It is unknown whether ECLS actively contributes to recovery through a decrease of the underlying higher level of intrinsic PEEP, or by avoiding ventilator-induced lung injury, or through an unforeseen mechanism, or ECLS simply provides support until a spontaneous improvement of bronchospasm occurs. Observational studies show that severe bronchospasm can abate suddenly after several days of pharmacologic therapy and support. Unfortunately, we can predict neither when nor if disease resolution will occur.[26] Nevertheless, ECLS remains a reasonable option for salvage treatment of adults with life-threatening status asthmaticus, and appears to be associated with favorable outcomes.

In conclusion, this case illustrates the effective use of ECLS for acute, severe, reversible respiratory failure due to asphyxic status asthmaticus, and to our knowledge this is the first reported case in which the patient's impending cardiopulmonary arrest was due to an unsustainable level of intrinsic PEEP. In managing patients with status asthmaticus, serial measurements of static pressures and peak inspiratory pressure should be used to guide and gauge the effectiveness of standard therapy and to predict when salvage treatment such as ECLS may be necessary to optimize the patient's outcome.

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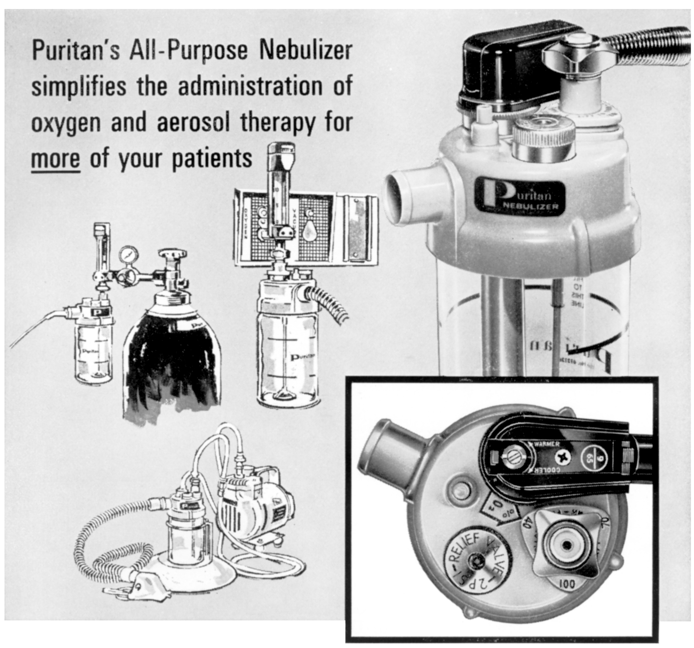

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