Gas Dialysis

A New Perspective on Extracorporeal Ventilation

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IN the critically ill patient or patient with hypoventilatory respiratory failure, there have been a number of methods to deal with the complication of hypercarbia. In both of these situations, the idea of tolerating hypercarbia with the label "permissive hypercapnia" has been advocated for over 20 yr.[1] In the acutely ill patient, acidosis ensues rapidly and is frequently well tolerated at moderate levels of carbon dioxide. However, at some point, this acidosis becomes profound enough that it must be addressed, and the work presented this month by Dr. Zanella *et al.*[2] represents a substantial potential advance in managing this situation.

The method used to address hypercapnia varies depending on the clinical condition of the patient. Typically, the first step is some form of mechanical ventilation (MV). If the patient is extubated, noninvasive positive-pressure ventilation is usually attempted. The patient is frequently kept without oral intake and potentially with bed rest in anticipation of worsening condition, endotracheal intubation, and invasive MV. If this occurs, the managing clinician should provide MV with a lung-protective ventilation strategy, consisting of low tidal volumes, reduced plateau pressures, and an adequate amount of positive end-expiratory pressure in an attempt to prevent ventilator-induced lung injury.[3]

However, as a patient's pulmonary status continues to deteriorate, the clinician is faced with balancing hypercarbia and acidosis with attempts to maintain lung-protective ventilation. In the modern era of MV, it is not uncommon to see patients with Pa_{CO_2} values in excess of 80 mmHg. These patients begin to suffer from profound acidosis and the clinician is faced with unfortunate options of increasing tidal volumes and pressures and inducing more lung injury or attempting to chemically buffer the acidosis. The use of buffering agents can introduce a variety of electrolyte disorders. In addition, there exists the theoretical possibility of rebound hypercapnia and acidosis from the metabolism of bicarbonate by carbonic anhydrase if sodium bicarbonate is the chosen buffering agent.

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To treat hypercarbia, there has been another option available to clinicians for over 30 yr with the use of extracorporeal technology.[4] Supplying patients with adequate extracorporeal oxygenation requires several liters of blood flow through a circuit. Distinctly lower flows are required to provide adequate extracorporeal carbon dioxide removal ($ECCO_2R$, pronounced e-kor). However, to date all extracorporeal technologies have required a minimum of approximately 500 to 1000 ml/min of blood flow through some form of an extracorporeal oxygenator to have a substantial clinical impact on carbon dioxide reduction. Systems have used a variety of technologies including venovenous access with mechanical pumps, whereas some commercial systems such as the Novalung iLA (Novalung GmbH, Heilbronn, Germany) in Europe advocate pumpless femoral arteriovenous circulation.

Existing systems have two requirements that introduce substantial risk to patients and limit the adoption of the technology. First, even though blood flow rates are substantially lower than 3 to 5 l/min, the 500 to 1000 ml/min flow rates still requires large venous access, substantially larger than a typical acute dialysis catheter. Such cannulae require specialized knowledge, can be challenging to place, and have been

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associated with substantial bleeding. In the case of arteriovenous cannulation, limb ischemia is a significant potential complication. Second, is the requirement for some form of systemic anticoagulation, which increases the bleeding risk even more, and is frequently contraindicated in critically ill patients.

The work presented in this month's ANESTHESIOLOGY by Dr. Zanella *et al.*[2] represents a substantial advance in extracorporeal ventilatory support. Through the infusion of lactic acid into the extracorporeal circuit, bicarbonate ion is converted to dissolved carbon dioxide which is almost completely cleared by an oxygenator. With this remarkable clearance of carbon dioxide, the investigators were able to provide a sustained substantial reduction in systemic arterial carbon dioxide with blood flow rates of 250 ml/min. Such rates are routinely used in continuous venovenous hemodialysis technology. This advance should permit carbon dioxide removal to be a far less invasive technology due to the use of a standard acute dialysis catheter and makes regional anticoagulation a viable option for the technology, minimizing the risk of bleeding. Due to the changes in the physical form of the technology, clinicians will no longer view extracorporeal ventilatory support as sophisticated extracorporeal membrane oxygenation (ECMO) or extracorporeal life support requiring a complex procedure, but as a much more manageable version of dialysis that happens to clear carbon dioxide rather than fluids and electrolytes.

Applications of this technology are multiple, but will generally fall into three categories: (1) acute ventilatory failure and prevention of MV, (2) lung-protective ventilation in severe respiratory failure, and (3) bridge to lung transplant in hypercarbic patients.

For patients with acute respiratory failure due to hypoventilation or asthma, it is conceivable that we may one day be debating the use of noninvasive positive-pressure ventilation, MV, or $ECCO_2R$ for support of patients. Such technology will allow ambulation, the organized weaning of support, and virtually eliminate the need for sedation. Historically, each of these measures has been associated with a reduced length of stay and improved outcomes.

In the patient with severe hypoxic respiratory failure undergoing advanced MV, the use of low-flow $ECCO_2R$ would enable the use of ultra-low tidal volumes. This should reduce the amount of barotrauma, atelectrauma, and subsequent ventilator-induced lung injury. Although exact indications will slowly be developed with the introduction of this technology and its ready accessibility, initial trials will probably address a patient population with severe respiratory acidosis despite the application of an appropriate lung-protective ventilation strategy.

Finally, in the carbon dioxide–retaining patient who is awaiting lung transplant, $ECCO_2R$ has already been used to bridge patients to their procedure, but usually only when they are nearing a requirement for invasive MV. Existing technology limits this to more advanced centers, typically with extracorporeal membrane oxygenation programs for patients suffering from profound hypoxia. Low-flow $ECCO_2R$ offers the potential for early support. With early intervention that does not require MV and bed rest, one anticipates that transplant candidates would be able to undergo physical therapy and rehabilitation before transplant, improving outcomes.

The data presented this month by Dr. Zanella *et al.* are clear step forward in the widespread adoption of $ECCO_2R$. However, support of a porcine model for 2 days with minimal lactic acidosis clearly requires human trials before generalized use. Additionally, this technology would also probably be contraindicated in patients with hepatic insufficiency due to the inability to metabolize the lactic acid load. Despite this limitation, the technology should be applicable to a wide array of patients.

In summary, Dr. Zanella *et al.* in Dr. Pesenti's lab should be commended for continuing their research in the low-flow $ECCO_2R$ domain. With this article, it is time for the technology to move from the animal model to human clinical trials, as low-flow $ECCO_2R$ has clear potential to benefit a multitude of patients suffering from respiratory failure.

Competing Interests

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