

Permissive Hypercapnia-Continuous Monitoring

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Alex Kline

Neonatology, Thomas Jefferson
University Hospital
Philadelphia, PA
USA



Kevin Dysart

Pediatrics, Columbus
Children's Hospital and The
Ohio State University
700 Children's Drive
Columbus, Ohio 43205
USA



Jay S. Greenspan

Pediatrics, Thomas Jefferson
University and the Nemours
Children's Clinics
Philadelphia
PA
USA

Neonatology, perhaps more than any other field in medicine, has undergone dramatic improvements in care over the last several decades. One of the main areas of advancement is the ability to mechanically ventilate premature infants with a variety of neonatal lung conditions.

As survival of premature infants has improved, much focus has been placed on the prevention of many of the more common neonatal morbidities, including bronchopulmonary dysplasia, retinopathy of prematurity, intraventricular hemorrhage and periventricular leukomalacia.

A recent area of interest has been the use of permissive hypercapnia to try and prevent bronchopulmonary dysplasia, the most common form of neonatal chronic lung disease.

Central to the concept of optimally ventilating infants is the need to monitor the infant's respiratory status,

not only in the first several days of life, but also beyond.

This article will discuss some of the most commonly used methods of following an infant's ventilation, and why it is so important to be able to monitor for acute changes as well as for more chronic maintenance.

Mechanical ventilation and bronchopulmonary dysplasia (BPD)

Mechanical ventilation of neonates was first successfully accomplished in the 1960s. Prior to this, there was often very little that could be done for extremely premature neonates. With the advent of neonatal mechanical ventilation, it became possible to better support infants with respiratory distress syndrome (RDS), later found to be due to surfactant deficiency [1].

It soon became apparent that while mechanical ventilation could be life saving, it often came at a price. In 1967, Northway *et al* first described a condition called

bronchopulmonary dysplasia (BPD), the most common form of neonatal chronic lung disease [2].

Over the last several decades, the pathophysiology of BPD has become increasingly understood, with factors such as volutrauma, barotrauma, atelectrauma and biotrauma all known to be contributing factors.

Much current research in the field of neonatology is focused on the prevention of BPD, as it still affects up to 30-40 % of preterm infants who require mechanical ventilation [3].

The injury cascade that ultimately lead to BPD has been shown to be initiated with even a few positive pressure breaths. Bjorklund *et al* have shown that as few as five artificial lung inflations with positive pressure with even modest tidal volumes can cause lung injury and affect lung function and compliance [4, 5].

Furthermore, even when given surfactant prior to the artificial breaths, only a few positive pressure breaths have still been shown to cause injury enough to affect pulmonary function [6].

The authors concluded that ventilating neonates, especially in the earliest moments, must be done as gently as possible to avoid unnecessary and potentially lasting damage.

Lung protective strategies

Over the years many strategies have been employed to try and prevent BPD by minimizing barotrauma, volutrauma and overdistention of an infant's fragile lungs. A generally accepted goal when ventilating neonates is to use only enough pressure to achieve a tidal volume of 4-6 mL/kg.

One of the problems in ventilating neonatal lungs is that they are a very dynamic organ early in life, with compliance and resistance changing constantly. Therefore, when using pressure-limited ventilation, the delivered tidal volume may vary during any given breath depending on the compliance, resistance and other factors.

An infant's arterial carbon dioxide pressure ($p\text{CO}_2$) is one of the best measures of an infant's ventilation. Historically, a $p\text{CO}_2$ in the range of 35-45 mmHg was set as the goal during mechanical ventilation.

One of the treatment strategies that has been employed over the last several years to try and decrease lung damage and subsequently BPD has been called permissive hypercapnia. This is discussed in depth in Dr Dysart's and Dr Greenspan's article in the October 2004 issue [9].

The central idea behind permissive hypercapnia is to accept higher CO_2 levels with the hope of minimizing unnecessary lung damage. The first studies of permissive hypercapnia were performed in adults with acute respiratory distress syndrome (ARDS).

These studies showed adults treated with a strategy to allow modest hypercapnia had increased survival and decreased time on a ventilator [7, 8].

Hypercapnia and hypocapnia

To date, the most appropriate CO_2 levels in infants have not been established. As opposed to the more traditional $p\text{CO}_2$ values of 35-45 mmHg, permissive hypercapnia allows $p\text{CO}_2$ values of 45-55 mmHg, as long as pH is >7.25 .

Unfortunately, the upper limits of safety for CO_2 levels have never been studied in the neonatal population. In clinical practice, it is common to have $p\text{CO}_2$ values in the 50s to 60s, as long as pH remains acceptable.

However, the potentially dangerous effects of hypercapnia relate more to the effect on pH, which must be maintained within more narrow margins. Any deviations in pH, particularly as related to acidosis, have effects on optimal function of the body's enzyme systems.

Some beneficial effects of hypercapnic acidosis are preservation of lung mechanics, attenuation of protein leakage, a reduction in pulmonary edema and improved oxygenation [11].

These beneficial effects are most likely related to a decrease in the degree of ventilator-associated lung injury on the neonatal lung, with a preservation in lung architecture and decreased trauma.

In addition, some potential non-pulmonary effects of hypercapnic acidosis include protecting the perinatal brain from hypoxic damage and shifting the oxygen-hemoglobin dissociation curve to the right, thereby improving tolerance to hypoxia at the tissue level [12].

As mentioned earlier, when ventilating neonates, it is essential to be able to accurately monitor CO₂ levels, as both hypocapnia and hypercapnia may have deleterious consequences.

Wiswell *et al* showed an association between hypocapnia and periventricular leukomalacia (PVL) in 67 infants treated with high-frequency jet ventilation. They showed that infants with PVL were more likely to have greater cumulative hypocapnia <25 mmHg during the first day of life [10].

This is significant because infants with PVL have been shown to have a higher incidence of cerebral palsy (CP). Dammann *et al* have demonstrated in a study of 799 infants that hypocarbia on the first day of life is associated with an increased risk of brain white matter injury [13].

In term infants, hypocapnia associated with treatment for persistent pulmonary hypertension of the newborn (PPHN) is associated with an increased risk of sensorineural hearing loss.

The brain injury associated with hypocapnic alkalosis is due in part to decreased cerebral blood flow due to cerebral vasoconstriction. Premature infants are particularly at risk for these effects due to their poorly regulated vascular supply and immature regulation of blood flow to the brain.

Monitoring of carbon dioxide levels

It is therefore essential to be able to accurately measure

an infant's CO₂ status, particularly in the first days of life, but also beyond. The gold standard for measuring the pCO₂(a) remains an arterial blood sample.

However, disadvantages to this method are the requirement for an indwelling arterial catheter, which is not always accessible, or peripheral arterial punctures, which are painful to the infant and at times difficult to obtain.

A blood gas sample is also really a look at the infant at a "*point in time*". As anyone who has worked with neonates can attest, an infant's respiratory status can change quickly. The narrow endotracheal tubes used in neonates often become dislodged, coated with secretions or plugged.

In addition, pulmonary mechanics such as compliance and resistance can change very rapidly with therapies such as surfactant, diuretics, or a re-intubation.

Also, blood gases are typically not obtained more often than every 1-2 hours, even in critically ill neonates, which means that hundreds or even thousands of ventilator breaths may be given between changes in ventilator settings.

Therefore, a way to continuously monitor an infant's respiratory status would be desirable. Pulse oximetry has greatly improved the way infants are managed, but this only reflects oxygenation and does not allow one to look at ventilation and carbon dioxide removal.

In general, the application of permissive hypercapnia to neonatal ventilation does not affect an infant's oxygenation or the way in which it should be monitored.

Capnography is one method in which carbon dioxide levels can be monitored in neonates. Capnography is the measurement of exhaled CO₂ and is also known as end-tidal CO₂ monitoring.

Because an infant's alveolar pCO₂ approximates the arterial pCO₂, by measuring a sample of alveolar gas one can get an estimate of the infant's arterial pCO₂.

Advantages to capnography are that it is inexpensive, easy to use and non-invasive. It has been shown to be accurate in healthy newborns; however, in sick newborns it is known to be less accurate [17].

End-tidal carbon dioxide monitoring is used in some nurseries to follow a trend in an infant's ventilation. Disadvantages to end-tidal CO₂ monitoring are that it is affected by parenchymal lung disease, ventilation-perfusion mismatching and cannot be used with high-frequency ventilation (HFV).

In HFV, the tidal volumes are less than the anatomic dead space, thus not making end-tidal monitoring possible. One application of capnography commonly used in our unit is to document successful endotracheal intubation.

With a colorimetric change in a small CO₂ detector placed on the end of an endotracheal tube, it is possible to confirm placement of the endotracheal tube in the trachea.

While an arterial blood gas requires either an arterial line or arterial puncture, it is often much easier to obtain a capillary blood gas (CBG). A heel puncture can obtain a sample of blood that is used to approximate arterial values.

By warming the heel, it is possible to partially arterialize the sample and gain a more accurate measurement of the blood gas values. When obtained properly, a CBG can closely approximate an arterial pH and pCO₂ value, but is less helpful in estimating the arterial pO₂.

Like with end-tidal CO₂ monitoring, CBGs are often used to follow a trend in an infant's ventilation.

Transcutaneous monitoring of CO₂ is also now being employed to more closely follow an infant's respiratory status. Like pulse oximetry, transcutaneous CO₂ monitoring allows continuous evaluation of an infant's ventilation.

Transcutaneous CO₂ monitors work through an electrode on the skin that heats the skin to 43-45 °C. This dilates capillaries, decreasing transit time and

allows diffusion of CO₂ from the blood vessel to the electrode. A correction factor is then used to adjust for the increased CO₂ production and the effects on CO₂ solubility due to the heat of the electrode.

Several studies have validated the accuracy of transcutaneous CO₂ monitoring. In a study by Tobias and Meyer, they found that in a cohort of pediatric ICU patients, the absolute difference between transcutaneous carbon dioxide and arterial carbon dioxide measurements was 4 mmHg or less in 96 of 100 values [14].

In another study by Tobias *et al* transcutaneous CO₂ levels and arterial CO₂ levels were measured in a group of infants and children following cardiothoracic surgery.

In 82 of 101 patients, the absolute difference in CO₂ levels was 2 mmHg or less [15]. Rauch *et al* used intermittent transcutaneous monitoring in a group of patients and found a mean difference of 1.94 mmHg between transcutaneous and arterial measurements [16].

Summary

Advances in neonatal mechanical ventilation have greatly contributed to the improved survival and long-term outcomes of infants admitted to an NICU with respiratory distress.

With increasing knowledge and awareness of the pathophysiology of neonatal lung injury, new strategies are being used to try and protect the infant's lung. In order to minimize the risk of unnecessary damage to the infant lung, it is crucial to be able to monitor both oxygen and carbon dioxide levels, not only in the acute phase of the illness, but also more chronically as well.

Capillary blood gases, end-tidal CO₂ monitoring and transcutaneous CO₂ monitoring are all ways in which an infant's ventilation can be monitored.

While each method has advantages and disadvantages, each can be used to help monitor the effectiveness of ventilation and help improve the outcome of these most vulnerable patients.

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