
TECHNIQUE

Assessment of Alveolar Function in Neonates on ECMO Using the Measurement of Net CO₂ Transfer by the Artificial Lung

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Abstract

The measurement of the net transfer of the CO₂ by the artificial lung (Delta Cap) during ECMO indicates the rate at which the alveoli are becoming functional and allows the prediction of when weaning can best begin. Usually, an infant with lung disease placed on ECMO will need to excrete most of his CO₂ production via the artificial lung. But as the alveoli heal, CO₂ will be removed in increasing amounts by the infant's own lungs. When the Delta Cap reaches zero, all of the infant's CO₂ production is being removed by his own lungs, an indication that he has adequate alveolar function to exchange O₂. A capnagraph is used to measure the CO₂ concentration of affluent and effluent sweep gas and the Delta Cap is determined by their difference.

Introduction

In the design of our ECMO system, a capnagraph was incorporated to measure the carbon dioxide (CO₂) concentration of the effluent sweep gas exiting the artificial lung. The capnagraph served as a safety feature to identify and prevent improper CO₂ titration of the sweep gas.

We quickly observed in our training exercises on lambs that the capnagraph measurements on the artificial lung could also reveal information about the respiratory status of the animal. The animals were kept sedated and arbitrarily ventilated during the entire ECMO training run. This permitted us to reduce or even stop the assisted ventilation to reproduce the "combat" situation that occurs with an actual ECMO baby; that is, total dependency on the ECMO circuit for oxygenation and CO₂ elimination.

An animal with normal lungs placed on venoarterial ECMO required very little CO₂ removal via the artificial lung. Even though the pulmonary blood flow is reduced on ECMO, pulmonary blood flow is sufficient to remove adequate amounts of CO₂ through ventilation. So, in order to prevent respiratory alkalosis, the CO₂ flow or titration to the artificial lung must be kept relatively high. Therefore, the affluent CO₂ sweep gas concentration measurement by the capnagraph must be kept

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equal to or greater than the effluent CO₂ sweep gas concentration.

If the ventilator is reduced or stopped and the animal can no longer exchange gas with its lungs, then the CO₂ titration must be reduced to prevent respiratory acidosis. If the CO₂ titration is not increased, the effluent CO₂ sweep gas concentration becomes higher than the affluent CO₂ sweep gas concentration because of the increased removal of CO₂ from the blood by the artificial lung. In fact, when the ventilator is entirely stopped, all the CO₂ produced by metabolism must be removed via the artificial lung.

This finding suggested that the degree to which a baby's lungs are able to exchange CO₂ could be measured indirectly and monitored constantly during the ECMO treatment. The clearance of CO₂ from human lungs depends on minute ventilation and available surface area (functioning alveoli), among other things. In fact, CO₂ clearance is more surface dependent than the exchange of oxygen (1). Measurement of CO₂ clearance by the artificial lung can be a useful tool in assessing surface area function in the infant lung.

In theory, the finite amount of CO₂ produced by the infant cannot be removed in excessive amounts by two different sources (the artificial lung and the human lungs) simultaneously and still maintain homeostasis. In a sick infant receiving ECMO and following reduction in ventilator settings, most, if not all, of the CO₂ must be excreted through the artificial lung. However, with human lung improvement, more CO₂ will be excreted by the human lungs. It should be noted that even the small amount of pulmonary blood flow occurring during pulmonary hypertension is adequate to excrete large amounts of CO₂. This improvement in CO₂ exchange may occur before any improvement in oxygenation can be seen (2).

Materials and Methods

The quantity of CO₂ transferred by the artificial lung can be

$$\text{*Partial Pressure of CO}_2 \times \text{Sweep Gas Flow} = \text{Volume of CO}_2$$

Barometric Pressure

Example: Cap-out = 30 mmHg CO₂

Barometric Pressure = 760 mmHg.

Sweep Gas Flow = 2500 cc/Min.

$30 \text{ mmHg} \times 2500 \text{ cc/Min.} = 97 \text{ cc/Min. CO}_2 \text{ flow}$

760 mmHg

easily calculated using the law of partial pressures*. Using the SciMed (a) 0.8 lung at a maximum gas flow of 2.5 liters per minute (l/min), each millimeter of mercury pressure (mmHg) of CO₂ measured difference between the affluent CO₂ concentration and the effluent concentration represents a net CO₂ transfer of 3.3 cubic centimeters per minute (cc/min) at a barometric pressure of 760 mmHg.

Delta Cap is the term we use to describe this net transfer of CO₂ by the artificial lung. Its measurement is made by taking the affluent CO₂ sweep gas partial pressure (Cap-in) and subtracting the effluent CO₂ sweep gas partial pressure (Cap-out). A negative Delta Cap means that CO₂ is being removed from the blood by the artificial lung. A positive Delta Cap means that CO₂ is being added to the blood by the artificial lung. A zero Delta Cap means no net CO₂ transfer by the artificial lung.

The relative severity of alveolar dysfunction can be assessed by comparing Delta Cap measurements and the infant's weight. A 2 kg. infant consumes approximately 6 cc/min/kg of oxygen (3) or 12 cc/min. Likewise, his CO₂ production will be approximately 12 cc/min. A Delta Cap of -2 mmHg in this infant receiving ECMO would indicate that the artificial lung is removing 6.6 cc/min of CO₂ (55% of the infant's CO₂ production). Hence, the infant's lungs must be removing 5.4 cc/min of CO₂ (45% of production).

A 4 kg. infant consumes 24 cc/min of O₂ and therefore generates approximately 24 cc/min of CO₂. A Delta Cap of -2 mmHg with this infant also indicates a removal of 6.6 cc/min of CO₂ by the artificial lung, but this represents only 28% of his total production. The other 72% must be excreted by the infant's lungs.

Infants with alveolar dysfunction will have high negative Delta Cap measurements. The Delta Cap becomes more negative during the first part of the ECMO treatment, reaching its most negative values between 18-70 hours into the run. This may require reduction of CO₂ titration into the sweep gas to prevent respiratory acidosis. With improving alveolar function, the Delta Cap will become less negative, approaching zero. An addition of CO₂ to the sweep gas may be needed to prevent respiratory alkalosis.

Infants with Primary Pulmonary Hypertension (PPHN) who have good lung volume and who have not sustained barotrauma prior to starting ECMO will have zero or positive Delta Cap measurements during the ECMO treatment because the problem is circulatory and not alveolar. Ventilator induced respiratory alkalosis is, in fact, a common treatment of PPHN (4) and demonstrates that even with reduced blood flow the infant's lungs can still transfer CO₂.

A simplified clinical interpretation of this Delta Cap concept in a child with alveolar dysfunction can be seen in Figure 1. Consider a 3 kg infant who uses about 18 cc/min of oxygen (O₂) and produces about 18 cc/min CO₂ who is placed on ECMO. For simplicity's sake, assume that his cardiac output is about 400 milliliters per minute (ml/min). Initially, 300 ml/min is

routed through the ECMO system and 100 ml/min goes through his lungs or shunts to the left side of his heart if there is pulmonary hypertension.

In Step 1, his first Delta Cap measurement is -6 mmHg. This indicates that virtually all 18 cc/min of CO₂ production is being removed by the artificial lung. Using a modified Fick formula the oxygen uptake (5) in the artificial lung can also be measured at approximately 18 cc/min. In other words, the entire gas exchange is occurring in the artificial lung.

In Step 2, as the lungs improve, the Delta Cap improves to -4 mmHg. We see that now only two-thirds of the CO₂ excretion is occurring via the artificial lung, indicating that his alveolar function has improved.

Accurate assessment of the O₂ exchange via the baby's lungs is impossible because we may only estimate pulmonary blood flow as being the difference between estimated normal cardiac output and the known ECMO pump flow (6). Assuming that one-third of the CO₂ production is being cleared by the baby's lungs then one-third of the estimated 100 ml/min blood flow going through the lungs is oxygenated. Assuming also that the mixed venous blood entering the lungs is 70% saturated (15 grams hemoglobin per 100 cc of blood) the pulmonary flow has the potential for picking-up approximately 6 cc/min of O₂. If only one-third of it is oxygenated, then the actual O₂ uptake is about 2 cc/min.

In Step 3, the Delta Cap improves to -2 mmHg. Now only one-third of the CO₂ production is being removed by the membrane lung. Two thirds of the CO₂ is being excreted by the infant's lungs. We assume that the oxygenation of the pulmonary blood flow is improving similarly so that now the O₂ uptake is 4 cc/min by way of the baby's lungs.

In Step 4, the Delta Cap reaches zero. There is no CO₂ being removed from the blood by the artificial lung. All 18 cc/min is being cleared by the human lungs. All of the presumed pulmonary blood flow is being oxygenated (6 cc/min.). Weaning can be initiated.

In Step 5, the lungs continue to improve, excreting more and more CO₂. The total CO₂ in the blood falls so that the gradient of CO₂ between the blood and the sweep gas is reversed. The Delta Cap becomes +2 mmHg. The efficient lung of the baby now must be countered by adding additional CO₂ to the sweep gas to prevent hypocapnea and respiratory alkalosis. The ECMO blood flow is reduced so that only one-half of the oxygenation is occurring in the artificial lung.

In Step 6, the ECMO blood flow is further reduced to 100 ml/min. Most of the oxygen uptake is occurring through the baby's lungs. Titration of CO₂ to prevent alkalosis continues and the patient is deemed ready to come off ECMO.

In Step 7, the patient is off ECMO and his lungs are exchanging 18 cc/min O₂ and CO₂ each.

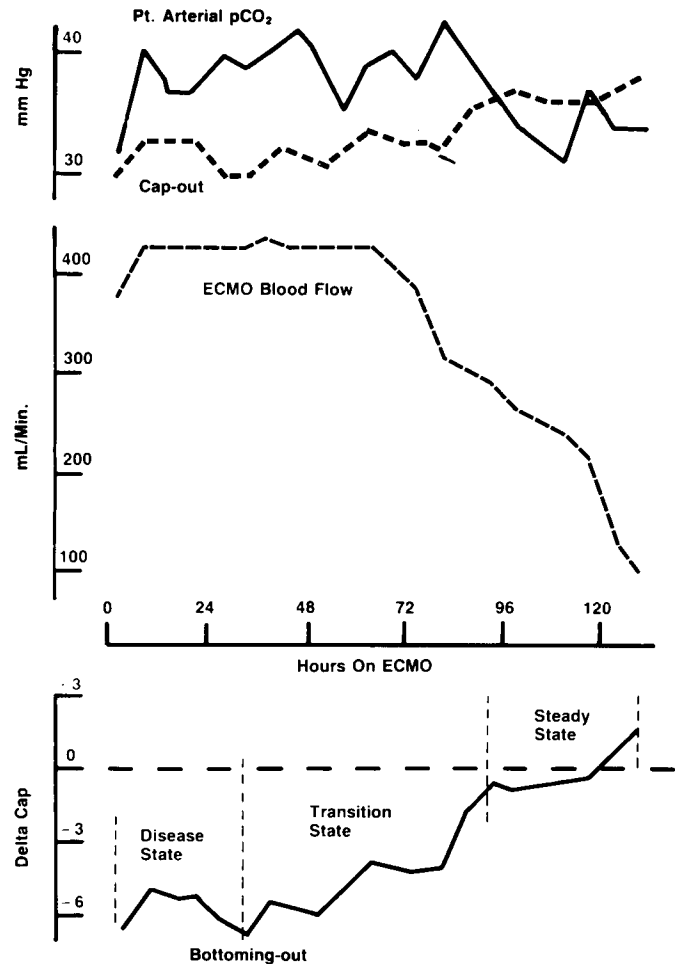
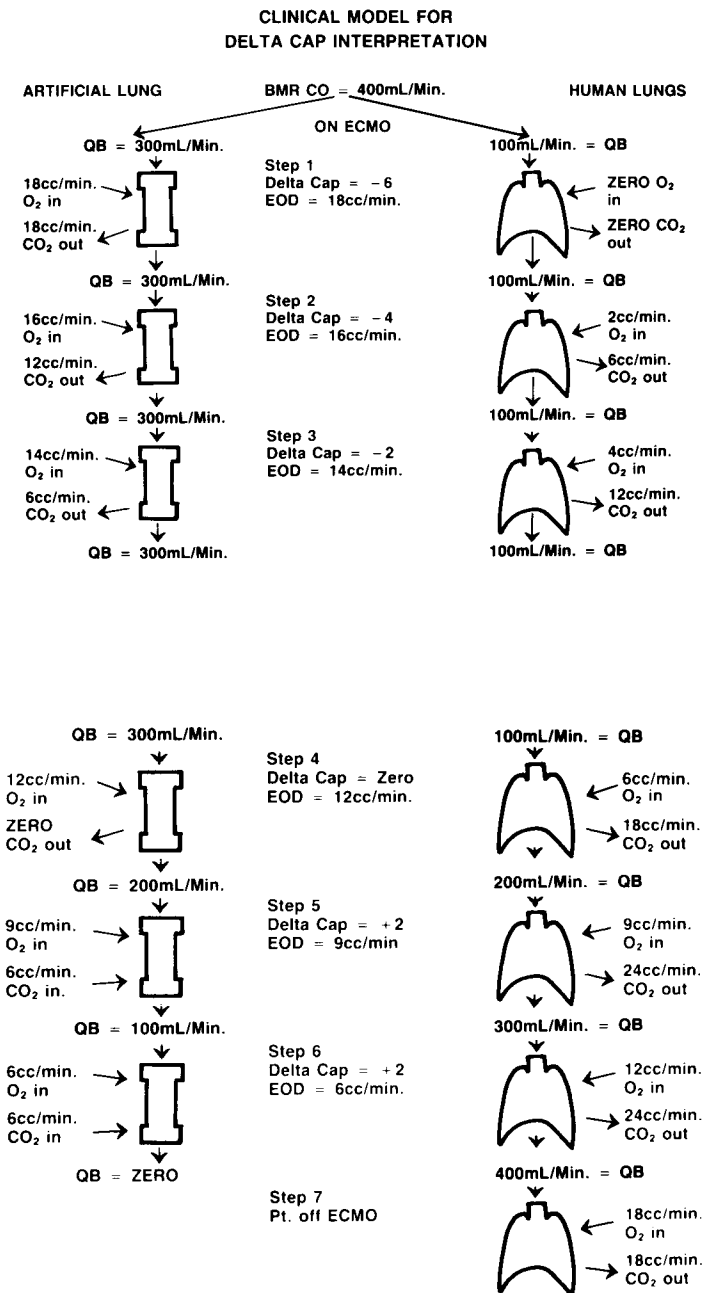
The Cap-in and Cap-out measurements are easily obtained. We use a Puritan-Bennett Datex CO₂ Monitor (b) (capnograph). We have found that: 1) its apnea alarm can be negated (the sweep gas flow is constant) 2), is very accurate, 3) it is easily calibrated and 4) it has worked for us hundreds of hours without breakdown. The CO₂ measurements read out digitally in mmHg or by bar graph in percentage of sweep gas flow.

a. SciMed Life Systems, Minneapolis, MN 55441

b. Puritan-Bennett Corp. of Mass., Wilmington, MA., 01887

Figure 1. Ideal model of gas exchange relationships between the artificial lung and the human lungs. Gas exchanges by the artificial lung can be accurately measured or calculated, but the values for human lungs can only be speculated. Premise: A 3 kg. infant with alveolar dysfunction. Approx. O₂ consumption = 18 cc/min. (6 cc/min/kg) Approx. CO₂ production = 18 cc/min. (6 cc/min/kg) Estimated Basal Metabolic Rate Cardiac Output (BMR/CO) = 400 ml/min., QB = Blood flow, EOD = ECMO Oxygen Delivery in cc/min.

Figure 2. Typical relationships of patient arterial pCO₂, Cap-out, ECMO blood flow and Delta Cap in a patient with alveolar dysfunction. The end of the disease state and the beginning of the transition state is marked by a "bottoming-out" of the Delta Cap at 33 hours on ECMO. The end of the transition state and the beginning of the steady state occurs when the Delta Cap becomes less than -1 mmHg. This is confirmed by the patient's arterial pCO₂ dropping below the Cap-out value.



The Cap-in measurements are made hourly. A straight tubing connector with a side luer port is installed in the affluent sweep gas line downstream from the site of CO₂ titration entry. The luer port is kept plugged unless a Cap-in measurement is being made. At that time, a line from the capnograph with a luer fitting is connected to the sweep gas line port, the reading is allowed to stabilize for five seconds and then recorded. The luer port is then replugged to prevent the sweep gas from escaping.

Cap-out values are monitored continuously as a safety precaution against improper sweep gas mixtures or sweep gas flow interruption. A 1/4 inch internal diameter extension tube is fitted on the gas exit port of the oxygenator. The tube is about eight inches long and has a straight connector with luer port installed in the center of the tube. The luer connector from the capnograph is attached to the luer port. The high sweep gas flow (2.5 l/min) ensures that the sample taken by the capnograph (150 cc/min) is not contaminated with room air. If the sweep gas flow changes significantly, the capnograph gives an inappropriate reading which informs the ECMO operator that there is a problem.

Results

The Cap-in and Cap-out measurements are taken hourly and the Delta Cap is calculated. The Delta Cap is then plotted on a graph along with the ECMO blood flow, patient arterial pCO₂ and Cap-out. Figure 2 represents a typical pattern in infants with alveolar dysfunction.

These graphs and the relationships of their components yield specific patterns for various types of illnesses. In most infants (excluding PPHN without barotrauma) three distinct phases occur during ECMO. The first is the Disease State. When the infant is first placed on ECMO, the Delta Cap value worsens until a bottoming-out occurs. In a 3 kg infant this value is usually -5 to -7 mmHg Delta Cap.

The second phase, Transition, begins when the Delta Cap improves; that is, becomes less negative. After a few hours of improvement, a slope is established enough so that a prediction of when the Delta Cap will reach zero can be made. As soon as the infant enters the Transition State weaning of the ECMO blood flow should begin.

The Steady State is the third phase and begins when the Delta Cap reaches zero. The blood flow should be aggressively weaned at this time. The ventilator should be adjusted so that the infant has control over his rate of respiration.

Discussion

Three other indicators are commonly used to help with determining the proper time to begin weaning. Improvement shown in chest radiographs can be very subjective. Arterial pO₂s are unreliable by themselves because they can be affected by shunting and by choice of sampling site. Improvement in mixed venous pO₂s is probably a good indicator of when to begin weaning, but its reliability can be affected by a left to right shunt. The Delta Cap measurement seems to be the most reliable indicator of the best time to begin weaning.

Unfortunately, Delta Cap measurements give no definite indication of improvement in the case of pulmonary

hypertension causing a right to left shunt. Continuing pulmonary hypertension as the primary component of the disease might be masked by RDS, MAS or barotrauma which were originally secondary components (7). Improvement in RDS, MAS or barotrauma can be graphically shown by Delta Cap measurements, but if the PPHN persists, the child will not be able to be weaned from ECMO even though the Delta Cap is zero or positive.

The Delta Cap measurements have potential for providing other important information during the ECMO run. The relative severity of the disease can be estimated by comparing the infant's weight to the Delta Cap value. Relative improvement can be estimated by comparing the "bottoming out" Delta Cap level to other improved values.

In certain instances, dramatic increases in metabolic rates can be seen. For example, an infant who normally is expected to bottom-out at -6 mmHg Delta Cap continues dropping to -12 mmHg. This not only indicates that his lung disease is very severe but that his CO₂ production (as well as his O₂ consumption) has doubled, possibly as a result of an infection. If this infant were to come off ECMO at such a time even for a short period, he would be at greater risk for hypoxic damage than if his Delta Cap were only -6 mmHg.

Delta Cap measurements may have a potential use in the management of Adult Respiratory Distress Syndrome, chemical aspiration, pneumonia, etc, in adults treated with ECMO.

Some authors believe that the best index of efficacy of alveolar ventilation is arterial CO₂ tension sustained by the human lung and PaCO₂ determination is therefore the most meaningful test of pulmonary function (8). The ability of the lungs to clear CO₂ is more indicative of alveolar function than arterial/alveolar pO₂ differences, and is being used increasingly as an element for determining survivability (9). Delta Cap measurements go four steps further by introducing quantitative values for relative severity, relative improvement, predictability, and differentiation between primary or secondary pulmonary hypertension.

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