Continuous blood gas monitoring in neonates and infants

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Introduction

The art and science of neonatology and pediatric intensive care have evolved dramatically during the last decades. Focus has changed from mere survival to survival without handicaps. Also in the discussion of long-term effects in survivors focus has widened: Brain lesions and cerebral damage are still in focus, but avoidance of lung damages is even more important. New knowledge of physiology and pathophysiology, new medications like surfactant and NO (nitric oxide), and new technologies like HFO (High Frequency Oscillation) and advanced laboratory analyses of small amounts of blood provide the clinician with an overwhelming weapon in the war against the illnesses of the neonate and the pediatric patient. However, sick newborns and infants still have a high risk of mortality and morbidity, and to minimize these risks the clinician has to be in control of the essential parameters. Among these are the blood gases, oxygen and carbon dioxide. Monitoring of oxygen and carbon dioxide is still a cornerstone in the management of the sick child, and with many of the new, very effective treatment modalities perhaps even more so than before. In recent years we have gained essential new knowledge of the influence of blood gases, especially carbon dioxide, on the organ function and damage to the organs. It has also been demonstrated how appropriate monitoring can minimize the risk of adverse outcome. Continuous monitoring of both oxygen and carbon dioxide is essential. Changes occur fast and may be left undetected for sufficient time for organ damage to develop if the clinician relies solely on intermittent monitoring like blood samples. This paper summarizes the essentials of continuous blood gas monitoring in neonates and infants and relates it to blood samples. The cases are constructed for teaching purposes, but they are all based on events during my more than 15 years in neonatal and pediatric intensive care.

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Monitoring $pCO_2$ - implications of low $pCO_2$

**Cerebral blood flow**

It is generally accepted that the arterial partial pressure of carbon dioxide $pCO_2$ (aB) strongly influences the cerebral circulation with a response time of a few minutes [1]. Decreasing $pCO_2$(aB) results in decreasing cerebral blood flow (CBF). Several studies have demonstrated a strong correlation between low $pCO_2$(aB) and adverse cerebral outcome [2,3]. It has not yet been established for how long the $pCO_2$(aB) must be below a certain value to cause brain damage, but there is reason to believe that the lower the value, the shorter the time needed to cause damage. At values of 22.5 mmHg (3.0 kPa) or less, damage can occur in as little as a few minutes, but also exposure to slightly higher partial pressures for a longer period of time may be dangerous [4]. For this reason alone, continuous monitoring of $pCO_2$ in any acutely ill child requiring ventilatory support should be incorporated as a standard of practice to reduce the risk of brain damage.

**Case**

A girl born after 25 gestational weeks at a district hospital. She was intubated immediately and given surfactant. Umbilical lines were inserted. The baby was ventilated with reasonable pressures and a rate of 40/min. Good oxygenation and circulation. Retrieval team arrived less than two hours after the birth and transported the girl for 85 minutes to the central university hospital. At departure, $pCO_2$(aB) was 37 mmHg (4.9 kPa), and ventilator rate was reduced. $pCO_2$ was not monitored during transport. At arrival at receiving hospital $pCO_2$(aB) was 21 mmHg (2.8 kPa) with blood pressure, heart rate and oxygenation being satisfactory. The low $pCO_2$ value places the baby at risk of cerebral damage and could have been avoided by monitoring $pCO_2$ during the transfer.
High Frequency Oscillation

High Frequency Oscillation (HFO) is a technique used in many centers for neonates as well as pediatric patients. Several studies of neonates have shown an increased risk of adverse cerebral outcome in patients treated with HFO, presumably due to inadvertent hyperventilation and low levels of $pCO_2$ [5,6]. The method is still popular despite the risks, as it seems to be protective against lung damage when compared to conventional ventilation. HFO is also effective in rescue situations in patients with hypercapnia during conventional ventilation. Significant reductions in $pCO_2$ can be observed within minutes after initiation of HFO. When HFO is used in combination with continuous monitoring of $pCO_2$ to avoid too low values of $pCO_2$, the risk of cerebral damage is minimized.

Case

A boy born at the age of 31 gestational weeks. Within the first 24 hours he developed severe pneumonia and septi-cemia due to group B streptococcus. Required high ventilatory pressures to keep $pCO_2$ at the desired level of 45-52 mmHg (6-7 kPa). HFO was therefore initiated with transcutaneous monitoring of $pCO_2$ and $pO_2$. During the first 30 minutes of HFO the ventilator was adjusted five times as tcp$CO_2$ dropped below the desired level. After one hour the transcutaneous values were stable, and a blood gas analysis revealed a $pCO_2$(aB) of 45 mmHg (6.0 kPa). There is little doubt that this patient could have suffered significant hypocapnia if not monitored continuously.

Hypocapnia and lung damage

Low $pCO_2$ before surfactant treatment as well as during ventilator treatment has been shown to be correlated to development of chronic lung disease of prematurity [7]. It is possible that the relation is due to high tidal volumes causing volutrauma of the lungs. In the preterm, volutrauma can be caused by just six inflations at birth [8]. Hyperventilation will result in hypocapnia. In the ventilated preterm it is therefore important to monitor $pCO_2$ continuously to minimize the risk of lung damage.

Monitoring $p$CO$_2$ - implications of high $p$CO$_2$

High values of $p$CO$_2$ may not be dangerous for the cerebral circulation of the neonate as no correlation between high $p$CO$_2$ and adverse outcome has yet been demonstrated. However, slight hypercapnia in animal studies has shown to have a protective effect on the brain suffering from ischemia [9]. Hypercapnia can result in acidosis, and in that case it may require treatment. Sudden upward changes in $p$CO$_2$ indicate changes in the condition of the child or complications to the treatment and must therefore lead to a careful evaluation of the situation.

**Case**

A boy, born at a gestational age of 26 weeks, initially treated with three doses of surfactant. On day 6 he remained on ventilator with low airway pressures and oxygen demands. In less than one hour he developed an increase in tcpCO$_2$ from 42 mmHg (5.6 kPa) to 51 mmHg (6.8 kPa) without any change in oxygenation. Careful evaluation of the condition revealed a prolonged expiratory phase and some hyperinflation of the chest. Repeated suctioning of the endotracheal tube removed some viscous plugs, and the situation normalized immediately. Without the continuous monitoring of $p$CO$_2$ it is likely that the condition would have progressed to a state endangering the baby.
Pneumothorax

Pneumothorax in the newborn has a significant mortality and morbidity. Early diagnosis is likely to improve the outcome. It has recently been shown that the diagnosis of pneumothorax is often late; median time from onset to clinical diagnosis was 127 minutes [10]. Transcutaneous monitoring of $pCO_2$ was shown to allow the diagnosis to be made earlier and thereby possibly reduce the risk of adverse outcome.

Case

A girl, born at a gestational age of 25 weeks, initially treated with two doses of surfactant. On day 3 she was still on ventilator with low airway pressures and oxygen demands. Within 30 minutes she developed an increase in tcpCO$_2$ from 38 mmHg (5.1 kPa) to 50 mmHg (6.7 kPa) without any change in oxygenation. The baby did not show a change in her condition following tracheal suctioning. Chest X-ray revealed right-sided pneumothorax, which was drained immediately, and her condition improved.

Permissive hypercapnia

Though still not proven beneficial in clinical, randomized studies of neonates, permissive hypercapnia is a treatment strategy used in many centers [11,12]. The exact level of $pCO_2$ to aim for is not well defined and varies between centers. When using permissive hypercapnia it is important to avoid too high levels of $pCO_2$ and acidosis [13]. During the initiation of permissive hypercapnia, but also later in the course, it is a safe method to use transcutaneous monitoring of $pCO_2$ to avoid excessive hypercapnia and acidosis.

References

Possibly the most important goal in the care of the sick neonate is to ensure an adequate oxygen supply to the tissues and organs of the baby. Hypoxia and ischemia are as dangerous in these patients as in any other patient, although the neonate is often more resistant to hypoxia than older patients. Hyperoxia, however, seems to be particularly endangering for the preterm neonate and more so than for older patients. This is presumably due to a lower antioxidant capacity [14].

Too much oxygen has been shown to reduce the cerebral blood flow for hours after normalization of oxygen status in newborn preterm infants. Toxicity to the lungs has also been demonstrated [15,16]. Hyperoxia must therefore be avoided, especially in preterm infants [17].

Little is known about optimal target levels for $pO_2(aB)$ and $sO_2(aB)$ in newborns with a large total concentration of hemoglobin and high amounts of fetal hemoglobin. It is important to keep in mind that fetuses develop and grow with $pO_2$ of 19-23 mmHg (2.5-3 kPa) and $sO_2$ of 65-70 %.

In newborns, term as well as preterm, high $ctO_2$ is obtained at low values of $pO_2$ due to a high concentration of hemoglobin and a large fraction of fetal hemoglobin.

Example

In a clinical, randomized study it was shown that 74 % of preterm neonates could be stabilized at birth without supplemental oxygen. Routine administration of oxygen to preterms at birth resulted in a significant reduction of cerebral blood flow lasting for several hours [15]. Several studies have shown that normal $sO_2$ in the first minutes after birth is less than 90 %.

The oxygen status of the neonate changes rapidly, and adequate monitoring therefore includes continuous monitoring.

Possibly, the best monitoring is a combination of tcp$O_2$ and pulse oximetry with intermittent arterial blood samples, including lactate measurements.

Pulse oximetry provides a fast response to changes in oxygen uptake and transport. The tcp$O_2$ offers trend information on the oxygen delivery to the tissues. Blood samples are necessary to correlate the non-invasively measured values to the arterial values and to get an in-depth overview of the oxygen status. Measurement of lactate is important to evaluate the adequacy of the oxygen supply to the tissues as the lactate production increases when oxygen supply is compromised, and anaerobic metabolism takes place.

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Methods of blood gas monitoring

Transcutaneous monitoring
Transcutaneous measurements of $pO_2$ and $pCO_2$ are based on heating of the skin under the electrode to increase the gas diffusion. Increase in temperature increases gas tensions, and the values are dependent on the electrode temperature. The electrode measures the gas tension in the underlying skin and not the arterial gas tension [18].

Transcutaneous $pO_2$ monitoring
Transcutaneous $pO_2$ provides trend information on the oxygen supply to the skin. The value is influenced not only by the arterial oxygen status, but also the peripheral circulation. This means that if the patient is hemodynamically stable, tcpO$_2$ will correlate well to arterial values, but this does not mean the values are the same. In the hemodynamically unstable patient, tcpO$_2$ will reflect changes in the circulatory status. One of the first physiological responses to circulatory compromise is peripheral vasoconstriction to maintain blood pressure. Skin perfusion is therefore often compromised before blood supply to central organs is impaired. Decreasing values of tcpO$_2$ are an early warning of onset of circulatory compromise and impaired oxygen supply to the tissues.

Transcutaneous $pCO_2$ monitoring
As the difference between arterial and venous values of $pCO_2$ is nominal, and carbon dioxide diffuses more easily than oxygen through tissue, tcpCO$_2$ is less influenced by the circulatory status than tcpO$_2$. Transcutaneous $pCO_2$ values are corrected to 37 °C (99 °F) and are normally close to arterial values.

End tidal CO$_2$ monitoring
This method can now be used even in preterm neonates as the dead space in modern monitors is reduced. However, the method can only be used in intubated patients, and it is only recommended for use in infants with no pulmonary or cardiac disease, i.e. for perioperative monitoring. In infants with cardio-pulmonary disease, end tidal CO$_2$ has been shown to have a poor correlation with arterial values and should therefore not be used [19]. In such patients, tcpCO$_2$ monitoring has been shown to be effective [20].
Pulse oximetry

Pulse oximetry provides continuous information on the utilization of oxygen transport capacity. Pulse oximeters are easy-to-use monitors of oxygenation and pulse rate. The method has, however, some limitations.

In a recent study it was found that even some new-generation pulse oximeters may miss significant numbers of hypoxemic episodes (5.4 %) as well as bradycardias (69 %) [21].

The inaccuracy of different pulse oximeters varies, and the algorithm used for calculation of \( sO_2 \) differs between brands, so the reported \( sO_2 \) from two pulse oximeters can be 2-3 \% apart. It is important to know the correlation between pulse oximeters used and values of \( sO_2 \) measured by CO-oximetry.

The correlation between \( sO_2 \) and \( pO_2 \) is depicted by the Oxygen Dissociation Curve (ODC). This correlation varies, and as the toxicity of too much oxygen depends on \( pO_2 \), pulse oximetry should never be relied on to detect hyperoxia [22]. Furthermore, pulse oximetry provides no information on \( pCO_2 \).

It is therefore recommended to combine pulse oximetry and transcutaneous monitoring. This increases the clinician’s ability to detect all deteriorations and provides important additional patient information.

Case

A term boy with birth asphyxia and meconium aspiration syndrome requiring HFO and surfactant instillation. At age 35 hours, with an \( FO_2(I) \) of 0.45, a mean arterial blood pressure of 45 mmHg (6.0 kPa), and an infusion of dopamine of 6 \( \mu g/kg/min \), the tcp\( O_2 \) started decreasing from 52 mmHg (6.9 kPa) to 44 mmHg (5.9 kPa) within less than an hour. All other parameters including blood pressure, pulse oximeter readings, and tcp\( CO_2 \) were stable. When tcp\( O_2 \) decreased with stable pulse oximeter saturation, it was most likely caused by peripheral vasoconstriction. The stable arterial oxygen status and normal lactate concentrations were confirmed by a blood sample. A bolus of saline was administered, leading to increase in tcp\( O_2 \). One hour later, tcp\( O_2 \) started to decrease again without changes in other values. An echocardiography revealed poor contractility of the heart, and infusion of dobutamine was initiated, leading to rapid normalization of tcp\( O_2 \).

This case provides essential combined monitoring information on the oxygen delivery and the circulatory status, allowing early treatment and avoidance of more severe compromise.
Umbilical artery catheters
Devices for invasive continuous monitoring of blood gases and pH have in recent clinical evaluations proven to be effective in providing reliable information on $\text{pO}_2(aB)$ and $\text{pCO}_2(aB)$ [23,24]. However, these devices are invasive and may therefore increase the risk of infections and can only be used for a limited time. This technique can, especially in patients where the skin condition makes transcutaneous monitoring difficult (typically extremely immature, newborn infants), be a valuable alternative to transcutaneous monitoring.

Blood samples
Arterial blood samples remain the standard of blood gas evaluation. However, the quality of blood sampling is essential for the results, and blood samples are always just momentary pictures of the status. The interpretation of blood samples is significantly improved when combined with continuous monitoring. Blood samples can have undesired side effects. Repeated samples may not only disturb and stress the patient, they may also cause the need for blood transfusion. The number of blood samples should therefore be reduced to a necessary minimum.

A recent study showed significant changes in cerebral circulation with impaired oxygenation in relation to sampling from umbilical artery catheters [25]. Care has to be taken to minimize this impairment. Capillary samples can, if collected correctly, to some extent substitute arterial samples. Capillary samples are, however, even more susceptible to preanalytical errors, and this must be kept in mind when results are interpreted [26]. Oxygen status and lactate in capillary samples may not correlate well with arterial values, especially in the child with compromised peripheral circulation.

Case
Preterm girl on ventilator. An arterial sample was needed. Before disturbing the patient, tc values were noted. Then the patient was approached and the sample collected. At the moment of sampling, the tc values were recorded again. This time tcpO$_2$ was 9 mmHg (1.2 kPa) lower and tcpCO$_2$ 6 mmHg (0.8 kPa) higher than before the disturbance. The blood sampling itself changed the blood gas values. When interpreting the blood gas results, the clinician could adjust for the acute changes.

Cases on transcutaneous monitoring in pediatric intensive care

Transcutaneous monitoring of $pO_2$ and $pCO_2$ can be used on all patient age groups: newborns as well as children [27, 28]. As the cerebro-vascular $CO_2$ reactivity in children is comparable to that of the newborn, the risk of hypcapnia-induced cerebral ischemia in PICU patients is the same as in NICU patients, and continuous monitoring of $pCO_2$ is necessary in both settings [29].

Case
A four-year-old girl with Pompe’s glycogen storage disease and progressive weakening of the respiratory muscles. During daytime her oxygenation was normal and $pCO_2$ at levels of 49-56 mmHg (6.5-7.5 kPa). Monitoring during sleep at night documented numerous desaturations and peaks of tcpCO$_2$ at 90-105 mmHg (12-14 kPa). Non-invasive positive pressure ventilation delivered by face mask was initiated, and the settings were guided by the continuous monitoring with pulse oximeter and transcutaneous $pO_2$ and $pCO_2$. She tolerated the mask ventilation, and the blood gas levels improved significantly. Several times leakage in the system, typically round the mask, was discovered by increase in tcpCO$_2$ without significant changes in oxygenation.
In cases like this, continuous monitoring of tcpCO$_2$ is a valuable additional tool for fast adjustment of ventilator settings and monitoring of ventilatory adequacy.
Case
A three-year-old boy with spastic tetraplegia and severe gastro-esophageal reflux, but normal lung function, underwent a gastric operation (fundublicatio) to prevent the reflux. Postoperatively epidural morphine and bupivacaine were administered continuously for pain palliation. The patient had oxygen administered on a face mask, and the respiratory function was monitored with a pulse oximeter, transcutaneous monitoring of \( \text{pO}_2 \) and \( \text{pCO}_2 \), and continuous monitoring of respiratory rate. Four hours postoperatively, the tcpCO\(_2\) gradually increased with stable oxygenation and minor decrease in the respiratory rate. A blood gas sample confirmed normal arterial oxygen parameters, but \( \text{pCO}_2 \) of 65 mmHg (8.6 kPa) and pH of 7.26. The infusion rate of the epidural medications was reduced, and three hours later the blood gas values had normalized. This case illustrates that in a patient with normal lung function, the oxygenation can remain normal despite significant hypoventilation. If the hypercapnia had not been detected by the continuous monitoring in this patient, the acidosis could have worsened to dangerous levels.

Case
A two-and-a-half year old boy suffering from acute lymphatic leukemia was admitted to PICU with ARDS (Adult Respiratory Distress Syndrome) due to infection with Pneumocystis Carinii. He required extreme ventilator settings and 100 % oxygen to reach just acceptable oxygenation. HFO was initiated, and within a few minutes his tcpCO\(_2\) began to fall, requiring repeated adjustments of the settings. However, oxygenation did not improve significantly, and it was decided to offer surfactant treatment before ECMO. Following surfactant instillation, \( \text{FO}_2 \) was reduced to 0.40 within 18 hours, and ECMO never became necessary. Then he deteriorated with steep increase in tcpCO\(_2\) to 90 mmHg (12 kPa) within less than an hour and without compromised oxygenation. A chest X-ray revealed no pneumothorax, but severe hyperinflation. Nothing could be obtained by tracheal suctioning, but as the situation got worse, the endotracheal tube was changed, and the situation normalized immediately. Dry secretions producing a one-way valve in the tube was found, and more secretions were removed from the bronchial tree by bronchoscopy.

The remainder of the course was uncomplicated, the boy was extubated after six days. Three years later he was well and without any sign of illness.

In this case, the transcutaneous monitoring proved invaluable both in adjusting HFO and in the detection of hypercapnia.

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Cases on transcutaneous monitoring in neonatal intensive care

Transcutaneous monitoring of $p_O_2$ and $p_CO_2$ is indicated whenever there is a risk of sudden changes in oxygenation or carbon dioxide status. Surfactant treatment, change in ventilator settings or ventilation strategy, weaning from ventilator, and after extubation are examples of some of the indications.

**Case**
A two-month-old girl with bronchopulmonary dysplasia needed a change of ventilator due to mechanical problems. The girl was manually ventilated while the ventilator was changed. Within less than three minutes, tcpCO$_2$ fell from 49 mmHg (6.5 kPa) to 39 mmHg (5.2 kPa). The ventilatory efforts were reduced and $p_CO_2$ normalized quickly. If not monitored, $p_CO_2$ could have decreased within minutes to levels endangering the cerebral circulation.

**Case**
A preterm infant, gestational age 25 weeks, birth weight 655 g, was on the second day of life weaned from ventilator following two courses of surfactant administration. With stable oxygenation, the rate and pressures on the ventilator were reduced gradually with only minor changes in tcpCO$_2$. No blood samples were collected. At an SIMV rate of 14/min and pressure of 15/4, the tcpCO$_2$ suddenly increased 11 mmHg (1.5 kPa) in 20 minutes without significant changes in oxygenation. The rate was increased to 18/minute and tcpCO$_2$ normalized. Six hours later the weaning could continue, and the child was extubated a further few hours later. No blood sample had been taken since weaning initially started. This example shows two things. First, it shows the importance of continuous monitoring of $p_CO_2$. This infant could have deteriorated significantly if the increase in $p_CO_2$ had passed unnoticed. Second, the need for blood samples during and after weaning can be reduced substantially.
Transcutaneous monitoring of $pO_2$ and $pCO_2$ is a user-friendly non-invasive method of monitoring the patient’s oxygen and carbon dioxide status. The combination electrode combines a Clark-type oxygen sensor and a Severinghaus-type carbon dioxide sensor. Following a quick (less than three minutes), automated calibration, the electrode is attached to the patient to begin the continuous monitoring following a short stabilization time. It is, however, more complicated to use transcutaneous monitoring of $pO_2$ and $pCO_2$ than to use a pulse oximeter. It is therefore important to follow the guidelines and instructions from the user’s manual, provided with the instrument.

Traditionally, there are concerns regarding transcutaneous electrodes: the heating of the skin and potential risk of burn wounds and pressure-induced necrosis. These risks can be eliminated or minimized by following some advice.

- The thinner the skin (i.e. the more premature the baby is) the lower temperature can be used. In adults and children, a temperature of 44 °C (111 °F) is recommended, and this temperature can be used for neonates and even preterm neonates. A temperature of 43.5 °C (110 °F) is sufficient in term neonates, and temperatures as low as 42 °C (108 °F) can be used, especially in very preterm infants. The lower the temperature, the less the risk of heat-induced skin changes. It is important to remember that when monitoring at the lower temperature, there will be a longer response time and greater difference between arterial and transcutaneous oxygen tensions.

- It is important to change electrode site every 3-4 hours; on patients with thin, gracile skin, every two hours, possibly every hour. This can be done by attaching two or three fixation rings and change position of the electrode between these. By not removing the fixation rings every time the electrode position is changed, the effect on the skin is minimized. The fixation ring should, however, be removed from the skin every 12 to 24 hours, depending on the condition of the skin.

- Direct pressure should never be placed on a transcutaneous electrode while on the patient. Additionally, the electrode should be placed so that the patient cannot lie directly on it. Both the above-mentioned incidences may invalidate the measurements and/or cause skin necrosis.

- In some patients it is not advisable to use transcutaneous monitors. This can be due to specific dermatological problems or edema of the skin like in hydrops.
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