2-2017

Measured and calculated variables of global oxygenation in healthy neonatal foals

David M. Wong
Iowa State University, dwong@iastate.edu

Kate L. Hepworth-Warren
Iowa State University

Beatrice T. Sponseller
Iowa State University, beatrice@iastate.edu

Joan M. Howard
Iowa State University, jmhoward@iastate.edu

Chong Wang
Iowa State University, chwang@iastate.edu

Follow this and additional works at: https://lib.dr.iastate.edu/vdpam_pubs

Part of the Large or Food Animal and Equine Medicine Commons, Veterinary Physiology Commons, and the Veterinary Preventive Medicine, Epidemiology, and Public Health Commons

The complete bibliographic information for this item can be found at https://lib.dr.iastate.edu/vdpam_pubs/116. For information on how to cite this item, please visit http://lib.dr.iastate.edu/howtocite.html.
Measured and calculated variables of global oxygenation in healthy neonatal foals

Abstract

OBJECTIVE To assess multiple central venous and arterial blood variables that alone or in conjunction with one another reflect global oxygenation status in healthy neonatal foals.

ANIMALS 11 healthy neonatal foals.

PROCEDURES Central venous and arterial blood samples were collected from healthy neonatal foals at 12, 24, 36, 48, 72, and 96 hours after birth. Variables measured from central venous and arterial blood samples included oxygen saturation of hemoglobin, partial pressure of oxygen, lactate concentration, partial pressure of carbon dioxide, and pH. Calculated variables included venous-to-arterial carbon dioxide gap, estimated oxygen extraction ratio, ratio of partial pressure of oxygen in arterial blood to the fraction of inspired oxygen, bicarbonate concentration, base excess, and blood oxygen content.

RESULTS Significant differences between arterial and central venous blood obtained from neonatal foals were detected for several variables, particularly partial pressure of oxygen, oxygen saturation of hemoglobin, and oxygen content. In addition, the partial pressure of carbon dioxide in central venous blood samples was significantly higher than the value for corresponding arterial blood samples. Several temporal differences were detected for other variables.

CONCLUSIONS AND CLINICAL RELEVANCE Results of this study provided information about several variables that reflect global oxygenation in healthy neonatal foals. Values for these variables in healthy foals can allow for comparison with values for critically ill foals in future studies. Comparison of these variables between healthy and ill foals may aid in treatment decisions and prognosis of clinical outcome for critically ill foals.

Disciplines

Large or Food Animal and Equine Medicine | Veterinary Physiology | Veterinary Preventive Medicine, Epidemiology, and Public Health

Comments

Measured and calculated variables of global oxygenation in healthy neonatal foals

David M. Wong DVM, MS
Kate L. Hepworth-Warren DVM
Beatrice T. Sponseller DVM, MS
Joan M. Howard VMD
Chong Wang PhD

Received November 16, 2015. Accepted June 3, 2016.

From the Departments of Veterinary Clinical Sciences (Wong, Hepworth-Warren, Sponseller, Howard) and Veterinary Diagnostic and Production Animal Medicine (Wang), College of Veterinary Medicine, Iowa State University, Ames, IA 50011.

Address correspondence to Dr. Wong (dwong@iastate.edu).

OBJECTIVE To assess multiple central venous and arterial blood variables that alone or in conjunction with one another reflect global oxygenation status in healthy neonatal foals.

ANIMALS 11 healthy neonatal foals.

PROCEDURES Central venous and arterial blood samples were collected from healthy neonatal foals at 12, 24, 36, 48, 72, and 96 hours after birth. Variables measured from central venous and arterial blood samples included oxygen saturation of hemoglobin, partial pressure of oxygen, lactate concentration, partial pressure of carbon dioxide, and pH. Calculated variables included venous-to-arterial carbon dioxide gap, estimated oxygen extraction ratio, ratio of partial pressure of oxygen in arterial blood to the fraction of inspired oxygen, bicarbonate concentration, base excess, and blood oxygen content.

RESULTS Significant differences between arterial and central venous blood obtained from neonatal foals were detected for several variables, particularly partial pressure of oxygen, oxygen saturation of hemoglobin, and oxygen content. In addition, the partial pressure of carbon dioxide in central venous blood samples was significantly higher than the value for corresponding arterial blood samples. Several temporal differences were detected for other variables.

CONCLUSIONS AND CLINICAL RELEVANCE Results of this study provided information about several variables that reflect global oxygenation in healthy neonatal foals. Values for these variables in healthy foals can allow for comparison with values for critically ill foals in future studies. Comparison of these variables between healthy and ill foals may aid in treatment decisions and prognosis of clinical outcome for critically ill foals. (Am J Vet Res 2017;78:230–238)

Shock, broadly defined as a failure to meet cellular metabolic demands, can result from failure of delivery or maldistribution of blood flow within the cardiovascular system. If hypoperfusion persists, tissue oxygen consumption decreases, which results in cellular dysoxia, anaerobic cellular metabolism, cell death, and multiorgan dysfunction. Clinical monitoring of shock in critically ill patients encompasses evaluation of several subjective and objective assessments and targeted therapeutic decisions to facilitate adequate oxygen delivery and restore aerobic cellular activity. By improving tissue oxygenation, the risk of multiorgan dysfunction, a cause of increased morbidity and mortality rates among hospitalized patients, can potentially be avoided. Toward this goal, specific therapeutic endpoints have been used to estimate adequacy of resuscitation in shock states, ranging from evaluation of noninvasive physical examination variables (eg, heart rate, capillary refill time, urinary output, and mental status) to more invasive measurements (eg, cardiac output and Svo2). Prospective clinical studies support the use of more invasive monitoring to guide early goal-directed therapy in critically ill people. Those studies were conducted with

ABBREVIATIONS

| BE | Base excess |
| BEna | Base excess in arterial blood |
| BEnv | Base excess in central venous blood |
| HCO3na | Bicarbonate concentration in arterial blood |
| HCO3nv | Bicarbonate concentration in central venous blood |
| O2Cta | Oxygen content in arterial blood |
| O2Ctv | Oxygen content in central venous blood |
| O2ER | Oxygen extraction ratio |
| PaCO2/FIO2 | Ratio between arterial partial pressure of oxygen and fraction of inspired oxygen |
| PcvO2 | Partial pressure of oxygen in central venous blood |
| PcvCO2 - Paco2 | Central venous–arterial difference in partial pressure of carbon dioxide |
| Saco2 | Arterial oxygen saturation |
| Scvo2 | Central venous oxygen saturation |
| Svo2 | Mixed-venous oxygen saturation |
the supposition that early hemodynamic assessment based on results of physical examination, vital signs, and urinary output would fail to detect persistent global tissue hypoxia, as might be observed during compensatory shock. Conversely, assessment and use of S\textsuperscript{v}O\textsubscript{2}, BE, pH, and arterial lactate concentration as therapeutic endpoints are arguably more valuable than physical examination variables and might help guide specific early goal-directed therapy to more effectively manipulate cardiac preload, afterload, and contractility to attain optimal balance between oxygen delivery and demand. It was concluded that early goal-directed therapy improved patient outcome for severe sepsis and septic shock (in-hospital mortality rate with early goal-directed therapy was 30.5%, compared with 46.5% without early goal-directed therapy). Interestingly, some follow-up studies refuted the benefits of invasive monitoring and early goal-directed therapy on the basis of a lack of difference in outcomes when protocol-based (ie, measurement of S\textsuperscript{v}O\textsubscript{2} and early goal-directed therapy) and standard-based resuscitation were used for septic shock, which has provided controversy in regard to the benefits of invasive monitoring and early goal-directed therapy in critically ill people.

Shock is commonly encountered in neonatal foals, primarily as a result of sepsis, but therapeutic endpoints in equine medicine are largely reliant on assessment of physical examination findings and blood lactate concentrations, which may fail to detect suboptimal oxygen delivery. Although the placement of a catheter in a pulmonary artery for measurement of S\textsuperscript{v}O\textsubscript{2} is impractical in most veterinary clinical settings, neonatal foals with sepsis or shock (or both) invariably require placement of a catheter in a jugular vein to initiate appropriate treatment. In these instances, a longer (35- to 40-cm) IV catheter routinely can be inserted to near the right atrium and used to collect central venous blood. Measurement of oxygen saturation in central venous blood is an acceptable replacement for measurement of oxygen saturation in mixed venous blood, although it overestimates S\textsuperscript{v}O\textsubscript{2} by 5%.

Measurement of Sc\textsuperscript{v}O\textsubscript{2} provides an estimate of the amount of oxygen that has been extracted from circulating hemoglobin by organs during the return of blood to the right side of the heart. In addition to Sc\textsuperscript{v}O\textsubscript{2}, several other variables investigated as markers of global oxygenation in humans may be applicable in foals. For example, P\textsubscript{ACO\textsubscript{2}} - P\textsubscript{A}CO\textsubscript{2} has been used to guide treatment of shock. Carbon dioxide is a normal terminal product of oxidative metabolism, and, in the absence of a vascular shunt, CO\textsubscript{2} concentrations in the venous blood must be higher than those in the arterial blood. In situations that result in anaerobic metabolism from oxygen debt, hydrogen ions are generated from hydrolysis of ATP to ADP and increased production of lactate. Hydrogen ions are buffered by bicarbonate present in cells; during this process, CO\textsubscript{2} is produced. The P\textsubscript{ACO\textsubscript{2}} is dependent on pulmonary gas exchange, whereas P\textsubscript{ACO\textsubscript{2}} is dependent on blood flow (ie, cardiac output) to remove CO\textsubscript{2} from the tissues. An inverse relationship exists between cardiac output and P\textsubscript{ACO\textsubscript{2}} - P\textsubscript{A}CO\textsubscript{2}, with increased P\textsubscript{ACO\textsubscript{2}} - P\textsubscript{A}CO\textsubscript{2} suggesting a decrease in blood flow. Other variables evaluated as markers of global oxygenation include P\textsubscript{AO\textsubscript{2}}, P\textsubscript{PCO\textsubscript{2}}, blood lactate concentration, and O\textsubscript{2}ER as well as blood gas variables (pH, bicarbonate concentration, and BE).

A paucity of clinical information currently exists with regard to basic global oxygen metabolism during sepsis and shock in equine neonates, and an equal lack of information exists with respect to monitoring foals with sepsis and shock. The objectives of the study reported here were to measure variables associated with global oxygen status as well as to compare results between central venous and arterial samples for several variables associated with systemic oxygenation. One or more of the evaluated variables subsequently may serve as a method for monitoring global oxygenation in ill foals.

Materials and Methods

Animals

Eleven university-owned Thoroughbred and Quarter Horse neonatal foals (5 colts and 6 fillies) were used in the study. Mean ± SD body weight was 52.2 ± 7.6 kg. All foals were considered healthy on the basis that the dam had an uncomplicated gestation and parturition and that physical examination variables of the foals were within acceptable limits. Foals were excluded if it was determined that they had inadequate passive transfer of immunity (serum IgG < 800 mg/dL, measured at 24 hours of age). Foals were kept with their dams during the entire study period; each dam and foal was housed in a box stall with access to small individual paddocks. The study protocol was reviewed and approved by the Iowa State University Institutional Animal Care and Use Committee.

Experimental design and sample collection

When foals were 12 hours old, anesthetic cream was topically placed on the lateral aspect of the left hind limb over the metatarsal dorsalis III artery. Foals then were sedated with diazepam (0.1 mg/kg, IV) and placed in right lateral recumbency on a padded mat. Hair over the left jugular vein was clipped, the skin was aseptically prepared, and 1 mL of lidocaine was administered SC over the jugular vein. A 16-gauge, 60-cm, single-lumen polyurethane catheter with a peel-away introducer was inserted into the jugular vein in the rostral third of the neck. Catheter length was estimated before insertion by measuring the distance from the catheter insertion site to the level of the caudal aspect of the scapula. The catheter was advanced until the tip of the catheter was located within 1 rib space of the cranial vena cava, which was confirmed by evaluation of a lateral thoracic radiograph. If the catheter was in the right atrium or
cranial to the cranial vena cava, the catheter was re­positioned and another radiograph was obtained to confirm proper placement. The catheter was in place with sutures, and patency was maintained by flushing 5 mL of heparinized saline (0.9% NaCl) solution through the catheter every 6 to 8 hours.

Blood samples were collected 10 minutes after foals were positioned in lateral recumbency. Approximately 0.5 to 1 mL of arterial blood was collected by use of anaerobic conditions from the metatarsal dorsalis III artery with a blood gas syringe containing lyophilized heparin. Subsequently, 10 mL of central venous blood was obtained anaerobically by use of the catheter in the cranial vena cava. For the central venous sample, ≥3 times the dead space volume of the catheter was withdrawn before sample collection. Approximately 1 mL of the central venous blood sample was placed by use of anaerobic conditions into a blood gas syringe containing lyophilized heparin, and the remaining central venous blood was split between a tube containing EDTA and a serum separator tube. The precollection blood was administered back to each foal via the IV catheter, and the catheter was flushed with heparinized saline solution. Arterial and central venous blood samples were collected from each foal at 12, 24, 36, 48, 72, 96, and 120 hours after birth.

Both the central venous and arterial blood samples were analyzed within 15 minutes after collection. Blood variables measured\(^a\) were [\(P_{cvO_2}\), \(P_{aoO_2}\), \(ScvO_2\), \(SaO_2\)], central venous lactate concentration, arterial lactate concentration, \(PcvO_2\), \(Paco_2\), central venous pH, and arterial pH. Variables calculated\(^b\) were \([PcvO_2 - Paco_2] = O_{2ER}\), \(O_{2Ctcv}\), \(O_{2Cta}\), \(HCO_3cv\), \(HCO_3a\), \(BEcv\), and \(BEa\). Equations used for calculation of some of these variables were as follows:

\[
O_{2ER} = (Sao_2 - ScvO_2)/Sao_2
\]

\[
O_{2Ctcv} = ([1.39 \times \text{hemoglobin concentration}] \times [Sao_2/100]) + (0.0031 \times PcvO_2)
\]

\[
O_{2Cta} = ([1.39 \times \text{hemoglobin concentration}] \times [Sao_2/100]) + (0.0031 \times Paco_2)
\]

\[
BEcv = (1 - [0.014 \times \text{hemoglobin concentration}]) \times \text{[HCO}_3\text{cv - 24]} + ([1.43 \times \text{hemoglobin concentration}] + 7.7) \times \text{[central venous pH - 7.4]}\]

\[
BEa = (1 - [0.014 \times \text{hemoglobin concentration}]) \times \text{[HCO}_3\text{a - 24]} + ([1.43 \times \text{hemoglobin concentration}] + 7.7) \times \text{[arterial pH - 7.4]}\]

In addition, 2 other variables were calculated by use of the following equations:

\[
\text{HCO}_3\text{cv - central venous pH} = \log_10(\text{HCO}_3\text{cv})/(\alpha \times PcvO_2)
\]

\[
\text{HCO}_3\text{a - arterial pH} = \log_10(\text{HCO}_3\text{a})/(\alpha \times Paco_2)
\]

where \(\text{pK} = 6.091\) and \(\alpha\) (ie, the solubility coefficient for CO\(_2\)) = 0.0307.

### Statistical analysis

All results were reported as mean ± SD. All measured and calculated blood variables (responses) were analyzed by use of repeated-measures ANOVAs. Sample, time, and the sample-by-time interaction were used as fixed effects, whereas foal was used as the subject of the repeated measures. Differences were assessed by use of the F test followed by the Tukey t test for multiple comparisons. For all analyses, values were considered significantly different at \(P < 0.05\).

### Results

No complications were associated with catheter placement or data collection, and vital signs remained within acceptable limits in all foals during the experimental period. Mean ± SD length of the central venous catheter (from catheter insertion site to the cranial vena cava) was 34.8 ± 2.5 cm. The \(Pao_2\) and \(SaO_2\) were significantly higher than the \(PcvO_2\) and \(ScvO_2\), respectively, at all time points. Furthermore, \(Pao_2\) was significantly lower at 12, 24, 36, and 48 hours, compared with the \(Pao_2\) at later times (Table I). The \(O_{2Cta}\) was significantly higher than the \(O_{2Ctcv}\) at all time points.

### Table 1—Mean ± SD values of oxygen saturation, partial pressure of oxygen, and oxygen content for blood samples obtained from 11 healthy foals at various times during the neonatal period.

<table>
<thead>
<tr>
<th>Age (h)</th>
<th>ScvO(_2) (%)</th>
<th>Sao(_2) (%)</th>
<th>PcvO(_2) (mm Hg)</th>
<th>Paco(_2) (mm Hg)</th>
<th>O(_2)Ctcv (mL of O(_2)/dL)</th>
<th>O(_2)Cta (mL of O(_2)/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>73.9 ± 9.2</td>
<td>92.2 ± 4.7(^a)</td>
<td>40.0 ± 5.3</td>
<td>64.6 ± 11.6(^a)</td>
<td>12.8 ± 2.1</td>
<td>16.1 ± 1.8(^a)</td>
</tr>
<tr>
<td>24</td>
<td>76.5 ± 4.8</td>
<td>94.8 ± 1.7(^b)</td>
<td>40.9 ± 4.0</td>
<td>69.9 ± 6.6(^b)</td>
<td>12.3 ± 1.2</td>
<td>16.6 ± 0.9(^b)</td>
</tr>
<tr>
<td>36</td>
<td>75.2 ± 4.6</td>
<td>93.4 ± 5.4(^c)</td>
<td>40.4 ± 3.5</td>
<td>69.3 ± 12.3(^c)</td>
<td>12.4 ± 1.2</td>
<td>15.5 ± 1.3(^c)</td>
</tr>
<tr>
<td>48</td>
<td>74.8 ± 4.5</td>
<td>95.1 ± 1.8(^d)</td>
<td>40.9 ± 3.3</td>
<td>72.1 ± 7.7(^d)</td>
<td>12.9 ± 1.7</td>
<td>16.5 ± 3.6(^d)</td>
</tr>
<tr>
<td>72</td>
<td>74.1 ± 5.1</td>
<td>96.5 ± 1.3(^e)</td>
<td>40.1 ± 3.8</td>
<td>78.8 ± 8.8(^e)</td>
<td>12.2 ± 1.4</td>
<td>16.3 ± 1.6(^e)</td>
</tr>
<tr>
<td>96</td>
<td>73.1 ± 8.9</td>
<td>96.3 ± 1.7(^f)</td>
<td>39.9 ± 6.0</td>
<td>78.2 ± 7.9(^f)</td>
<td>11.9 ± 1.7</td>
<td>16.3 ± 1.7(^f)</td>
</tr>
<tr>
<td>120</td>
<td>73.7 ± 6.9</td>
<td>96.2 ± 1.2(^g)</td>
<td>39.8 ± 3.9</td>
<td>78.4 ± 5.9(^g)</td>
<td>12.0 ± 2.0</td>
<td>16.1 ± 1.2(^g)</td>
</tr>
<tr>
<td>All ages</td>
<td>74.5 ± 1.1</td>
<td>95.0 ± 1.7</td>
<td>40.2 ± 0.6</td>
<td>—</td>
<td>12.4 ± 0.4</td>
<td>16.2 ± 0.4</td>
</tr>
</tbody>
</table>

\(^a\)Within a row, value differs significantly \((P < 0.05)\) from the corresponding value for the central venous variable. \(^b\)Within a column, value differs significantly \((P < 0.05)\) from the value at 12 hours. \(^c\)Within a column, value differs significantly \((P < 0.05)\) from the value at 24 hours. \(^d\)Within a column, value differs significantly \((P < 0.05)\) from the value at 36 hours. \(^e\)Within a column, value differs significantly \((P < 0.05)\) from the value at 48 hours.

—\(^f\) = Not determined.
Table 2—Mean ± SD values of various measured and calculated variables for blood samples obtained from 11 healthy foals at various times during the neonatal period.

<table>
<thead>
<tr>
<th>Age (h)</th>
<th>PcvCO₂ (mm Hg)</th>
<th>Paco₂ (mm Hg)</th>
<th>PcvCO₂ − Paco₂ (mm Hg)</th>
<th>O₂ ER (%) (mm Hg)</th>
<th>Lactate-cv (mmol/L)</th>
<th>Lactate-a (mmol/L)</th>
<th>Pao₂/FIO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>45.2 ± 2.9</td>
<td>42.4 ± 2.9</td>
<td>2.9 ± 2.2</td>
<td>198 ± 9.6</td>
<td>2.5 ± 0.9</td>
<td>2.5 ± 0.9</td>
<td>300 ± 57</td>
</tr>
<tr>
<td>24</td>
<td>45.2 ± 2.9</td>
<td>42.4 ± 2.9</td>
<td>2.9 ± 2.2</td>
<td>198 ± 9.6</td>
<td>2.5 ± 0.9</td>
<td>2.5 ± 0.9</td>
<td>300 ± 57</td>
</tr>
<tr>
<td>36</td>
<td>46.4 ± 3.8</td>
<td>41.3 ± 4.0</td>
<td>5.1 ± 1.9</td>
<td>192 ± 7.0</td>
<td>1.4 ± 0.3†</td>
<td>1.4 ± 0.4†</td>
<td>332 ± 59</td>
</tr>
<tr>
<td>48</td>
<td>45.6 ± 3.4</td>
<td>41.0 ± 3.0</td>
<td>4.6 ± 2.1</td>
<td>209 ± 3.8</td>
<td>1.4 ± 0.4†</td>
<td>1.4 ± 0.5†</td>
<td>345 ± 37</td>
</tr>
<tr>
<td>72</td>
<td>46.2 ± 2.8</td>
<td>40.8 ± 2.8</td>
<td>5.3 ± 1.4</td>
<td>22.4 ± 4.3</td>
<td>1.6 ± 0.7</td>
<td>1.7 ± 0.7</td>
<td>376 ± 42†</td>
</tr>
<tr>
<td>96</td>
<td>44.2 ± 2.5</td>
<td>38.8 ± 2.9†</td>
<td>5.4 ± 3.0</td>
<td>24.1 ± 9.2</td>
<td>1.5 ± 0.6†</td>
<td>1.5 ± 0.4†</td>
<td>374 ± 38†</td>
</tr>
<tr>
<td>120</td>
<td>43.9 ± 3.5</td>
<td>38.5 ± 2.4†</td>
<td>5.4 ± 3.0</td>
<td>23.6 ± 6.8</td>
<td>1.4 ± 0.2†</td>
<td>1.4 ± 0.2†</td>
<td>375 ± 28†</td>
</tr>
<tr>
<td>All ages</td>
<td>44.6 ± 1.1</td>
<td>—</td>
<td>4.5 ± 1.0</td>
<td>21.3 ± 2.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Lactate-a = Arterial lactate concentration. Lactate-cv = Central venous lactate concentration.

See Table 1 for remainder of key.

Table 3—Mean ± SD values of BE, bicarbonate concentration, and pH for blood samples obtained from 11 healthy foals at various times during the neonatal period.

<table>
<thead>
<tr>
<th>Age (h)</th>
<th>BEcv (mEq/L)</th>
<th>BEa (mEq/L)</th>
<th>HCO₃cv (mmol/L)</th>
<th>HCO₃a (mmol/L)</th>
<th>pHev</th>
<th>pHa</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>5.1 ± 1.9</td>
<td>4.5 ± 1.8</td>
<td>29.6 ± 2.0</td>
<td>28.6 ± 2.1</td>
<td>7.422 ± 0.024</td>
<td>7.433 ± 0.015</td>
</tr>
<tr>
<td>24</td>
<td>4.7 ± 2.2</td>
<td>3.7 ± 2.0</td>
<td>28.8 ± 2.3</td>
<td>27.3 ± 2.1</td>
<td>7.432 ± 0.025</td>
<td>7.445 ± 0.024</td>
</tr>
<tr>
<td>36</td>
<td>5.0 ± 2.1</td>
<td>3.9 ± 2.0</td>
<td>29.3 ± 2.3</td>
<td>27.8 ± 2.3</td>
<td>7.425 ± 0.022</td>
<td>7.433 ± 0.022</td>
</tr>
<tr>
<td>48</td>
<td>4.7 ± 1.6</td>
<td>3.9 ± 1.8</td>
<td>29.3 ± 2.0</td>
<td>27.8 ± 2.0</td>
<td>7.416 ± 0.025</td>
<td>7.435 ± 0.017†</td>
</tr>
<tr>
<td>72</td>
<td>5.3 ± 2.4</td>
<td>4.3 ± 2.6</td>
<td>30.0 ± 2.5</td>
<td>28.1 ± 2.7</td>
<td>7.416 ± 0.022</td>
<td>7.441 ± 0.021*</td>
</tr>
<tr>
<td>96</td>
<td>4.2 ± 2.1</td>
<td>3.4 ± 2.0</td>
<td>28.6 ± 2.1</td>
<td>26.6 ± 2.6†</td>
<td>7.415 ± 0.020</td>
<td>7.452 ± 0.032*</td>
</tr>
<tr>
<td>120</td>
<td>4.1 ± 1.7</td>
<td>3.4 ± 1.9</td>
<td>28.5 ± 1.9</td>
<td>26.7 ± 2.3</td>
<td>7.418 ± 0.021</td>
<td>7.459 ± 0.020†</td>
</tr>
<tr>
<td>All ages</td>
<td>4.7 ± 0.4</td>
<td>3.9 ± 0.4</td>
<td>29.2 ± 0.6</td>
<td>27.6 ± 0.7</td>
<td>7.421 ± 0.006</td>
<td>7.442 ± 0.010</td>
</tr>
</tbody>
</table>

pHa = Arterial pH. pHev = Central venous pH.

See Table 1 for remainder of key.

The Pao₂/FIO₂ was significantly higher at 72, 96, and 120 hours, compared with the value at 12 or 24 hours (Table 2). There was no significant difference between arterial and central venous lactate concentrations at any time point. The arterial lactate concentration was significantly higher at 12 hours, compared with the arterial lactate concentration at 36, 48, 96, and 120 hours. The central venous lactate concentration was significantly higher at 12 hours, compared with the central venous lactate concentration at 24, 36, 48, 96, and 120 hours. At all times, PcvCO₂ was significantly higher than the corresponding Paco₂. The Paco₂ was significantly higher at 12 hours, compared with Paco₂ at 96 and 120 hours. No significant differences in PcvCO₂ − Paco₂ or O₂ ER were detected at any time.

Central venous pH was significantly lower than arterial pH at 48, 72, 96, and 120 hours. The HCO₃cv was significantly higher than HCO₃a at 96 hours (Table 3).

There was no significant effect of time on PcvCO₂, O₂ Gcv, O₂ Cta, ScvO₂, SaO₂, PcvCO₂, PcvCO₂ − Paco₂, O₂ ER, central venous pH, arterial pH, HCO₃cv, HCO₃a, BEcv, and B Ea. Therefore, a mean value over time for each variable was calculated (Tables 1–3).

Discussion

Clinical and hemodynamic variables such as heart rate, blood pressure, urine output, and central venous pressure can be unreliable or late indicators of inadequate tissue perfusion and, in some situations, may provide limited guidance for timely treatment. In the study reported here, investigation into the use of central venous and arterial blood variables associated with global oxygenation in healthy neonatal foals was conducted to establish baseline values. The subsequent objective will be to compare similar global oxygen variables for ill foals, with the intent of improving treatment and the ability to determine prognosis in situations such as sepsis and septic shock in neonatal foals.

In the present study, placement of a central venous catheter into the cranial vena cava in healthy neonatal foals was technically easy to accomplish, and the catheter was easy to maintain for the 5-day study period. Inflammation or skin irritation was not detected at the catheter insertion site, and adverse effects attributable to catheter placement were not encountered.

Mean body weight of the foals was 52.2 kg, and the mean length of the catheter from the insertion site to the cranial vena cava was 34.8 cm. Ideally, catheter placement in the cranial vena cava should be confirmed with radiography; however, if radiography is not available, we suggest (on the basis of subjective observation) that length of the catheter to reach the cranial vena cava can be reasonably estimated by measuring the distance from the catheter insertion site to the caudal aspect of the scapula.

The SVO₂ reflects the amount of oxygen remaining in blood in the pulmonary artery, including blood
from the cranial and caudal vena cava, coronary sinus, and right side of the heart, after all the tissues of the body have consumed oxygen, and it is a representative index of global tissue oxygenation. The \( S\text{v}O_2 \) has been used in critical care settings for people to aid in treatment decisions (eg, assessing resuscitation, cardiac function, and systemic oxygen balance) as well as for determining a prognosis. Moreover, assessment and monitoring of \( S\text{v}O_2 \) can be more reliable than the use of physical examination variables in patients with compensated shock, whereby noninvasively measured variables can fail to detect the presence or severity of shock. However, collection of mixed-venous blood samples requires placement of a catheter in a pulmonary artery, which traverses 2 heart valves. This procedure is invasive and technically challenging and can be associated with complications, including catheter-associated infections, increased risk of arrhythmias, and, rarely, rupture of the pulmonary artery. Thus, measurement of \( S\text{v}O_2 \) has become less popular in the human critical care field.

In contrast, measurement of \( S\text{v}O_2 \) in samples obtained from the cranial vena cava has been advocated as a surrogate for \( S\text{v}O_2 \). The main factors that influence \( S\text{v}O_2 \) are the concentration of hemoglobin, \( S\text{a}O_2 \), cardiac output, and oxygen consumption. Theoretically, if hemoglobin concentration, \( S\text{a}O_2 \), and oxygen consumption are kept constant, \( S\text{v}O_2 \) reflects cardiac output. In healthy people, \( S\text{v}O_2 \) ranges from 73% to 82%, with a high or low \( S\text{v}O_2 \) suggestive of potential pathological conditions. A low \( S\text{v}O_2 \) indicates increased oxygen extraction from hemoglobin and typically suggests inadequate oxygen delivery or increased oxygen consumption, whereas a high \( S\text{v}O_2 \) can result from impaired oxygen utilization and may represent an inability of cells to extract oxygen, mitochondrial defects, or microcirculatory shunting in sepsis. Evaluation of blood lactate concentrations and \( P\text{v}CO_2 - P\text{a}CO_2 \) may help differentiate the underlying cause of alterations in \( S\text{v}O_2 \).

In the study reported here, no significant difference in \( S\text{v}O_2 \) was detected during the experimental period (12 to 120 hours); mean ± SD \( S\text{v}O_2 \) over all times was 74.5 ± 1.1% (range, 52% to 87%). Mean values of \( S\text{v}O_2 \) in healthy neonatal foals were similar to those measured in healthy people (76 ± 6%). In humans with sepsis, a target treatment endpoint of \( S\text{v}O_2 \) > 70% has been suggested, but prospective trials in ill foals will be necessary to evaluate the use of \( S\text{v}O_2 \) as a treatment endpoint. In dogs with experimentally induced hypovolemia, low or decreasing \( S\text{v}O_2 \) and high or increasing \( P\text{v}CO_2 - P\text{a}CO_2 \) were detected after administration of furosemide, which reflected changes in global oxygen balance and altered microcirculatory blood flow in hypovolemia. As expected in the present study, \( S\text{a}O_2 \) was significantly higher at all times than was \( S\text{v}O_2 \); mean \( S\text{a}O_2 \) over all times was 95 ± 1.7%, which is similar to measurements in healthy neonatal foals reported elsewhere.

In relation to \( S\text{v}O_2 \) and \( S\text{a}O_2 \), values for the partial pressure of oxygen in mixed-venous blood in recumbent neonatal (birth to 14 days of age) foals have been reported, with a mean ± SD value of 40.5 ± 0.5 mm Hg over the 14-day study period. Mean \( P\text{v}CO_2 \) reported in the present study (40.2 ± 0.6 mm Hg) for central venous blood was similar to that previously reported for mixed-venous blood. In the present study, mean \( P\text{a}O_2 \) was significantly lower at 12 hours, compared with the \( P\text{a}O_2 \) at several later time points (ie, 48, 72, 90, and 120 hours). This pattern has been observed in other studies and is attributed to the change in gas exchange efficiency that developmentally occurs in foals during the first week after birth.

As would be expected in healthy foals, \( P\text{v}CO_2 \) was significantly higher than \( P\text{a}CO_2 \) during the study period, and values were similar to \( P\text{a}CO_2 \) measured in samples obtained from the pulmonary vein of neonatal foals and healthy adult dogs. The \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) has been used as a marker of global hemodynamic status and might have use for the detection of low blood flow states in ill neonatal foals. An increase in \( P\text{v}CO_2 \) results when cellular oxidation overwhelms the body’s buffering systems. Although \( P\text{a}CO_2 \) is variable and dependent on pulmonary gas exchange, \( P\text{v}CO_2 \) is dependent on blood flow (ie, cardiac output) to remove CO2 from tissues. Thus, an increase in \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) can reflect decreased blood flow and has been reported in critically ill humans with severe sepsis, heart failure, hypovolemia, or other low-flow states. Evaluation of blood lactate concentrations and \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) has been recommended for conditions in which oxygen uptake is insufficient because of microcirculatory or mitochondrial defects (ie, severe sepsis) that result in a falsely elevated \( S\text{v}O_2 \); in this situation, an increase in \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) may help clinicians detect inadequate oxygen delivery. No difference in \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) was noted over time in the healthy foals of the present study; mean ± SD \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) over all times was 4.5 ± 1.0 mm Hg, which is similar to the \( P\text{v}CO_2 \) - \( P\text{a}CO_2 \) in healthy people (< 5 mm Hg) and healthy dogs (5.8 mm Hg). The \( O_2\text{ER} \) is the amount of oxygen removed from the blood by the tissues. Oxygen extraction increases in situations of decreased oxygen delivery (ie, shock), tissue hypoxia, or lactic acidosis or as a result of increased metabolic demand. A strong negative correlation between \( O_2\text{ER} \) and \( S\text{v}O_2 \) has been detected in humans: as hemoglobin becomes more desaturated, an increase in oxygen extraction occurs, which results in a decrease in \( S\text{v}O_2 \). When oxygen delivery decreases below the threshold to maintain oxygen consumption via increased oxygen extraction, consumption becomes delivery dependent and tissues begin to produce lactate, with lactic acidosis typically accompanying an \( O_2\text{ER} > 50\% \). Conversely, a decrease in \( O_2\text{ER} \) can be observed if tissue oxygen consumption decreases or if tissues cannot use oxygen; this situation may be associated with an abnormal increase in \( S\text{v}O_2 \). If the tissues
are not capable of extracting oxygen (ie, shunting of blood or cell death), venous blood may have a high oxygen content despite persistent cellular hypoxia. The O2ER has also been used to help identify patients with fatal conditions, especially those with ScvO2 > 70%. The mean O2ER for all times in the foals of the study reported here was 21.3%, which is comparable to that reported for dogs (20.5%) and healthy people (25%).

Lactate is the end product of glycolysis, with the arterial lactate concentration historically used as the reference value for assessment of tissue hypoxia or dysxia. However, it has been suggested that venous and arterial lactate concentrations can be used interchangeably. Venous blood samples can typically be collected more rapidly and are technically easier to collect, compared with arterial blood samples, which has spurred investigation of the suitability of venous blood lactate concentrations as an early indicator of sepsis. In a study, the mean difference between venous and arterial lactate concentrations in people was 0.54 mmol/L, which suggests that lactate concentrations in peripheral venous blood can be an appropriate substitute in septic patients. In another study, investigators found a strong correlation (r = 0.96) between arterial and peripheral venous blood lactate concentrations, with venous blood lactate concentrations more effective than arterial lactate concentrations for use in detecting severe sepsis. Other investigators compared central venous and arterial blood lactate concentrations and reported a mean difference in central venous-to-arterial lactate concentrations of 0.08 mmol/L. Conversely, a difference between arterial and venous lactate concentrations has been found (mean venous lactate concentration was 1.1 mmol/L higher than the corresponding arterial lactate concentration in people admitted to an emergency department). In comparison, a slightly higher arterial lactate concentration, compared with the venous blood lactate concentration, was detected in people with sepsis. In the study reported here, the central venous lactate concentration was comparatively similar to values for peripheral venous samples obtained from healthy foals. A significant difference was not detected between the central venous and arterial lactate concentrations in the present study, which suggested that central venous and arterial lactate concentrations can be used interchangeably for healthy neonatal foals. Both arterial and venous lactate concentrations have been evaluated in neonatal foals with sepsis; however, to our knowledge, no studies have been conducted to compare peripheral venous or central venous lactate concentrations with arterial lactate concentrations in ill foals.

Studies have also detected a relationship between the degree of acidosis and mortality rates in critically ill patients. Blood pH is commonly evaluated during blood gas analysis and is a cornerstone for assessment of acid-base status. In contrast to pH values measured in adult horses, in which no difference was detected between venous and arterial pH, the foals of the study reported here had a significantly lower central venous pH, compared with the arterial pH, at 48, 72, 96, and 120 hours. Other variables have been used to assess hemodynamic failure. For example, inadequate oxygen delivery to tissues during sepsis or other conditions associated with hypoperfusion may be identified by an increase in lactate concentrations, but a number of unmeasured acidic compounds can also be present during these conditions and perhaps better detected by assessment of BE or serum HCO3 concentration. Base excess has been used as a marker of tissue perfusion and adequacy of resuscitation as well as a predictor of mortality rates. Low (more negative) BE values at admission have been associated with higher mortality rates, and improvement of BE in patients with severe sepsis and septic shock has been a strong predictor of a better outcome. In addition, BE has been suggested as a surrogate for blood lactate concentration when a lactometer is not available, with BE -4 mEq/L correlating with a lactate concentration > 3 mmol/L. In a study involving ill neonatal foals, BE < 3.9 mEq/L predicted hyperlactatemia (lactate concentration > 5 mmol/L) with good sensitivity and specificity. Base excess also has been used as an indicator of metabolic acid-base disturbances. In the study reported here, a significant difference between BEcv and BEa was not detected, with mean values of 4.7 and 3.9 mmol/L, respectively. In addition to BE, serum HCO3 concentrations have also been suggested as a method for evaluation of acid-base status as well as a surrogate for BE. Measurement of serum HCO3 concentration is more readily available because these concentrations are routinely measured during serum biochemical analysis, whereas blood gas analysis is not always available. In studies that involved evaluation of human patients in intensive care units, serum HCO3 concentration had a strong correlation (r = 0.857) with BE and was a reliable indicator of metabolic acidosis. In many ways, these variables (lactate concentration, BE, and HCO3 concentration) are different facets of the same process (ie, perturbation of the acid-base equilibrium as a result of the nonvolatile acid load originating from dysfunctional cells [lactate] or dead cells [intracellular strong acid content higher than plasma content]). However, depending on the degree of perturbation during critical illness and availability of diagnostic testing, one or more of these specific variables may help guide future resuscitation efforts in ill foals and could potentially aid in determining prognosis.

The PAO2/FIO2 was implemented in the 1990s to improve standardization of research and criteria for more accurate determination of disease severity and prognosis as it relates to acute respiratory distress syndrome. This ratio facilitates evaluation of the respiratory system by comparing PAO2 with the amount of inspired oxygen and is part of the inclusion criteria for acute lung injury and acute respiratory distress.
syndrome. The suggested \( Pao_2/\text{FiO}_2 \) values in clinically normal animals are similar to those in the study reported here, although the mean \( Pao_2/\text{FiO}_2 \) at 24 hours in the present study was 300 mm Hg, whereas the suggested ratio in the consensus statement was > 350 mm Hg. This difference may in part have been attributable to the fact that data used to calculate \( Pao_2/\text{FiO}_2 \) in the consensus statement were based on values from foals in a standing position (compared with recumbent foals in the present study) or differences in instrumentation.

Data for the study reported here will help to validate the recommended consensus values for \( Pao_2/\text{FiO}_2 \) in neonatal foals and provide additional time points (36, 72, and 120 hours) for evaluation of \( Pao_2/\text{FiO}_2 \).

Oxygen content in blood is needed to calculate other variables associated with global oxygenation, such as oxygen delivery and oxygen consumption. In the present study, there was no effect of time on \( O_2\text{Cta} \) and \( O_2\text{Ctcv} \); thus, the mean value over time for these 2 variables was 16.2 and 12.4 mL/dL, respectively. These values in healthy foals are similar to, but slightly less than, those measured in healthy humans (18 to 20 mL/dL for \( O_2\text{Cta} \) and 13 to 16 mL/dL for \( O_2\text{Ctcv} \)) and dogs (O2 Cta, 18.5 mL/dL; O2 Ctcv, 14.7 mL/dL). Oxygen content is greatly impacted by hemoglobin concentration, which differs among reports. The hemoglobin content factor used to estimate hemoglobin oxygen content differs from 1.31 to 1.39, with a mid-range value of 1.34 used in many studies; in the study reported here, a value of 1.39 was used.

One limitation of the present study was that only 11 healthy foals were used to investigate the variables associated with systemic oxygenation. Ideally, data for a larger number of healthy foals would have been collected. In addition, foals were sedated with diazepam at 12 hours of age to facilitate catheter placement. Although foals appeared to regain normal mentation and activity by the time catheter placement was complete (approx 30 to 45 minutes), it is possible that residual effects of diazepam may have impacted some of the variables to a slight degree. Finally, it has been reported that collection of blood from recumbent foals alters results for some of the variables (eg, venous partial pressure of \( O_2 \), venous partial pressure of \( CO_2 \), and \( Pao_2 \)). In the study reported here, both central venous and arterial blood samples were collected while foals were recumbent because this would most likely be the position of ill foals in a clinical situation. In addition, collection of arterial blood samples from a foal in a standing position would be extremely difficult. Despite these limitations, this study provided values for central venous and arterial blood variables that can be used for comparison with measurements obtained in future research investigations and clinical patients.

Many of the variables investigated in this report interact or impact one another; thus, it is unlikely that a single variable will be a panacea. However, future investigation and use of one or more of these variables for ill foals may facilitate early detection of critical clinical conditions (ie, shock or sepsis), help guide treatment decisions (eg, when to initiate provision of supplemental oxygen, vasopressors, or IV fluids), and provide prognostic information.

**Footnotes**

- PHOx Ultra analyzer, Nova Biomedical, Waltham, Mass.

**References**


34. Tánczos, K., Nemeth, M., Molnar Z. The multimodal concept of hemodynamic stabilization. *Front Public Health* 2014;2:34.


[Footnotes and references not included in natural text representation]


