Changes in central venous pressure and blood lactate concentration in response to acute blood loss in horses

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Objective—To evaluate selected hemodynamic, blood gas, and biochemical responses to mild to moderate acute blood loss in standing, awake horses.

Design—Prospective study.

Animals—7 healthy mares.

Procedures—Each horse was restrained in standing stocks, and its head was maintained in a neutral position; sedatives and tranquillizers were not administered. During a 1-hour period, blood was collected into collection bags by use of a suction pump. The rate of blood collection was approximately 16 mL/kg/h (73 mL/lb/h). Thirty minutes after blood collection, the blood was readministered at the same rate. Central venous pressure (CVP), central venous blood gas, blood lactate concentration, and heart rate were measured at baseline (after placement of catheters), after removal of blood, and after readministration of blood.

Results—In response to blood loss, CVP decreased and blood lactate concentration increased significantly, compared with baseline values; heart rate and results of central venous blood gas analysis did not change significantly. After readministration of blood, CVP returned to baseline value and blood lactate concentration approached baseline value.

Conclusions and Clinical Relevance—Changes in CVP and blood lactate concentration appear to be early indicators of hypovolemia in horses, which may represent acute blood loss in trauma patients; these variables should be monitored to assess the potential need for blood transfusions. These variables can be used to monitor responses of horses to blood transfusions when whole blood is administered as the replacement fluid. (J Am Vet Med Assoc 2006;229:1458–1462)

There is a paucity of information available on the hemodynamic and biochemical responses to acute blood loss in standing, awake horses. To the authors’ knowledge, only 1 study has evaluated the effects of acute blood loss on arterial and pulse pressures and heart rate. Additional indices, such as blood lactate concentration, were not described in that study. In 2 studies, the cardiopulmonary effects of hemorrhage in anesthetized horses were evaluated, and in another study, the effects of hemorrhage on hematologic, serum electrolyte, and blood gas variables were assessed in a similar group of horses. The effects of a polymerized hemoglobin product in horses with chronic blood loss have also been evaluated, but the horses in that study had normovolemic anemia because of volume replacement with colloids.

For any species, understanding the cardiovascular and metabolic responses to blood loss is important in the decision-making process for the need for blood transfusions. Knowledge of those responses will aid in estimating the volume of blood lost from the body and assessing the need for transfusions or additional cardiovascular support in a clinical setting. In horses, hemoperitoneum, hemorrhage from enterotomies or wounds, or as a result of guttural pouch mycosis, and renal hematuria represent clinical examples of acute blood loss; increased understanding of the associated physiologic responses would benefit clinicians attempting to treat those conditions.

Current opinions regarding transfusion triggers in horses are anecdotal and have been extrapolated from human medicine. These include thresholds for systolic blood pressure, heart rate, mucous membrane color, pulse pressure, and Hct. Tachycardia is a variable finding, and assessment of Hct is neither sensitive nor specific because of splenic contraction. End points of blood transfusion administration are also undetermined in horses and based primarily on clinician experience. Because little information regarding the response to blood loss in horses is available, research in this area is needed.

The purpose of the study reported here was to evaluate selected hemodynamic, blood gas, and biochemical responses to mild to moderate acute blood loss in standing, awake horses. The goal was to identify early indicators of blood loss and means of monitoring effects of blood transfusions in horses. It was anticipated that the findings of this study would aid in establishing guidelines for clinical blood transfusion triggers and end points and result in an improved understanding of the physiologic responses to hemorrhage in horses. The hypothesis of the study was that

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CVP</td>
<td>Central venous pressure</td>
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<tr>
<td>PcvO₂</td>
<td>Central venous oxygen tension or partial pressure</td>
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<td>PcvCO₂</td>
<td>Central venous carbon dioxide tension or partial pressure</td>
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acute blood loss is marked by notable alterations in CVP, blood lactate concentration, and venous blood gases in horses.

Materials and Methods

Seven university-owned mares were included in the study. They were considered healthy on the basis of physical examination findings. The horses weighed 465.2 to 578.9 kg (1,023.4 to 1,273.6 lb) and included Thoroughbreds, Quarter Horses, Arabsians, and horses of mixed breeding. The study was approved by the University Animal Use and Care Administrative Advisory Committee of the University of California, Davis. Feed was withheld from all horses for 12 hours prior to and during the study to reduce variability in gastrointestinal fill and abdominal pressure.

Each horse was restrained in standing stocks, and its head was maintained in a neutral position during the experiment. Sedatives and tranquilizers were not administered at any time during the study. For catheter placement, 2% lidocaine (0.5 to 1 mL) was injected to create a subcutaneous bleb over each jugular vein. A 10-gauge polytetl catheter was placed in the left jugular vein and used for blood removal and replacement. A 3.5-F, 60-cm central venous catheter was placed in the right jugular vein according to manufacturer's directions and used for collection of central venous blood samples and CVP measurements. The tip of the catheter was located within the vena cava, as verified by oscillations in the fluid meniscus with respiration. Catheters that are placed extrathoracically will not undergo oscillations in the fluid meniscus with respiration. The catheters were not placed in the right ventricle, as verified by the magnitude of pressure fluctuations. The CVP measurement was made at the end of expiration. A 30-F Foley urinary catheter was placed in the bladder of each horse and attached to a closed urinary collection system.

Procedures—After placement of catheters, baseline blood samples were collected from each horse for analysis. Baseline measurements of CVP and heart rate were also obtained. Total urine volume obtained prior to blood removal was recorded, and urine production throughout the experimental procedure was recorded every 5 minutes. Blood removal was performed by use of a suction pump, and blood was collected into collection bags containing anticoagulant citrate dextrose solution in a ratio of 9 parts blood to 1 part citrate. During a 1-hour period, blood was removed and collected at a rate of approximately 16 mL/kg/h (7.3 mL/lb/h; volume removed, 16 mL/kg [range, 7.4 to 9.3 L]). Thirty minutes after the end of blood collection, the removed blood was administered back to the horse at the same rate during a 1-hour period. Blood samples were collected for measurement immediately following completion of blood removal and again following completion of blood replacement.

Blood sample analysis—At the aforementioned times, a 1-mL sample was collected into a syringe containing heparin for blood gas analysis and measurement of blood lactate concentration. The samples were stored anaerobically on ice until analysis by use of a commercial analyzer within 20 minutes of collection.

CVP—Extension tubing was used to connect a plastic water manometer to 1 port of the central venous catheter via a 3-way stopcock. The 20-cm mark was placed at the point of the shoulder as a reference because of anticipated negative readings. The manometer was affixed to the side of the stocks to maintain consistency in height and placement among readings.

Statistical analysis—All values are reported as median, range, and mean ± SD. A nonparametric ANOVA (Friedman) with a post hoc Dunn test was used for comparisons of medians. Median CVP and heart rate at baseline, immediately after removal of 16 mL of blood/kg (3.6 mL of blood/lb), immediately after removal of 16 mL of blood/kg, 30 minutes after removal of 16 mL of blood/kg, and after replacement of 16 mL of blood/kg were compared. Median blood lactate concentration and results of central venous blood gas analysis (ie, values of Pco2, Pvcv, standard base excess, pH, and bicarbonate concentration) at baseline were compared with values immediately after removal of 16 mL of blood/kg and after replacement of 16 mL of blood/kg. A value of P < 0.05 was considered significant.

Results

The catheter placement and technique for CVP measurement were straightforward, and there were no associated complications in any horse.

Immediately after removal of 16 mL of blood/kg, CVP had decreased (median, –1.6 cm H2O; range, –4 to 5 cm H2O; mean ± SD, –0.1 ± 3.8 cm H2O) significantly (P < 0.01) from baseline value (median, 7 cm H2O; range, 5 to 14.8 cm H2O; mean, 8.2 ± 3.5 cm H2O; Figure 1). The blood loss–associated decrease from baseline CVP value persisted through the 30-minute period after completion of blood removal (median, –1.6 cm H2O; range, –13 to 10 cm H2O; mean, –1.2 ± 7.0 cm H2O; P < 0.01). Median blood lactate concentration at baseline (0.6 mmol/L; range, 0.4 to 1.1 mmol/L; mean, 0.7 ± 0.2 mmol/L) and immediately after maximal blood loss (1.35 mmol/L; range, 0.5 to 6.7 mmol/L; mean, 2.2 ± 1.0 mmol/L) was also significantly (P < 0.05) different. Median Pco2 at baseline was 32.8 mm Hg (range, 27.4 to 36.2 mm Hg; mean, 32.3 ± 1.2 mm Hg); immediately after removal of 16 mL of blood/kg, this value had decreased to 28.8 mm Hg (range, 24.0 to 33.1 mm Hg; mean, 28.9 ± 1.4 mm Hg), but this difference was not significant (P = 0.14). Compared with baseline values, there were no significant changes in central venous blood pH, Pcv (bicarbonate concentration, or standard base excess immediately after maximal blood loss. Median heart rate increased from baseline value with blood loss (baseline, 41.5 beats/min [range, 36 to 44 beats/min; mean, 41 ± 2.8 beats/min]; immediately after removal

Figure 1—Mean ± SD CVP before (baseline, B) and during removal and replacement of blood (16 mL/kg [7.3 mL/lb]) in 7 awake, standing horses. Blood was withdrawn or replaced during a 1-hour period; measurements were performed after removal of 8 mL of blood/kg (3.6 mL of blood/lb), immediately after removal of 16 mL of blood/kg, 30 minutes after removal of 16 mL of blood/kg, and after replacement of 8 mL of blood/kg, and after replacement of 16 mL of blood/kg. **Values with different letters were significantly (P < 0.01) different.
of 16 mL of blood/kg, 32.5 beats/min [range, 32 to 61 beats/min; mean, 49.7 ± 11.5 beats/min]; and after replacement of 16 mL of blood/kg, 40 beats/min [range, 32 to 48 beats/min; mean, 40.4 ± 5.0 beats/min]). However, there was no significant change in heart rate at any time point throughout the study. The urine volume prior to blood removal was 0 because the bladder of each horse had been emptied with the urinary catheter. Urine output did not vary among time points but was low throughout the study period (2.5 hours); median total volume was 0.2 L (0.15 mL/kg/h [0.068 mL/lb/h]).

After replacement of 16 mL of blood/kg, median CVP increased to near baseline value (6.1 cm H2O; range, 2.2 to 14.5 cm H2O; mean, 7.9 ± 4.3 cm H2O), which was a significant (P < 0.05) change from the values obtained immediately after maximal blood loss and after the 30-minute holding period (Figure 1). After completion of blood volume replacement, the median value of PCV 0.3 (30.7 mm Hg) approached baseline value (32.8 mm Hg), although this was not significantly different from the value after removal of 16 mL of blood/kg. Median blood lactate concentration decreased immediately after replacement of 16 mL of blood/kg (1.1 mmol/L; range, 0.4 to 5.2 mmol/L; mean, 1.56 ± 1.65 mmol/L); however, this value was not significantly different from the value after maximal blood loss (1.35 mmol/L; range, 0.5 to 6.7 mmol/L; mean, 2.2 ± 1.0 mmol/L) and did not return to baseline concentration (0.6 mmol/L). Blood volume replacement did not significantly affect central venous blood pH, PCO2, bicarbonate concentration, or standard base excess. After completion of the study, the horses appeared healthy and were returned to their normal housing environment.

Discussion

The purpose of the present study was to evaluate the effects of mild to moderate blood loss (volume of 16 mL/kg) in standing, awake horses. As determined by use of indicator dilution, the total blood volume of horses ranges from 62.4 to 109.6 mL/kg (28.4 to 49.8 mL/lb).15,16 On the basis of this range, the horses in our study had 15% to 26% of their blood volume removed during a 1-hour period. This degree of blood loss would be categorized as class I (15% to 19% loss) or II (20% to 25% loss) in a classification scheme of hemorrhagic shock in humans.17 A volume of 16 mL/kg was selected because it is the amount commonly removed from blood donor horses for provision of transfusions and is generally considered a physiologically safe amount of blood loss for the donors. It also allows for study of early clinical and clinicopathologic indicators of blood loss in horses. A study20 in which the influence of acute hemorrhage on hemodynamic parameters in pigs was evaluated involved a similar volume (20 mL/kg). The minor alterations in various variables detected in our study likely reflect the relatively modest amount of blood loss and were expected findings. More marked hemodynamic and biochemical changes likely would have developed with larger losses of blood. Despite the relatively small volume of blood loss, there was a decrease in CVP and increase in blood lactate concentration (compared with baseline values), indicating that these variables may be sensitive, early indicators of blood loss in horses. The lack of changes in the blood gas results of our study is similar to the blood loss–associated findings of Schmall et al21 in an investigation of anesthetized horses.

Results of the present study indicated that CVP decreases with acute blood loss in horses, even with only modest losses (ie, 16 mL/kg). This is an expected change because CVP reflects venous blood volume status and decreases during hypovolemia. Other factors affecting CVP include venous tone and cardiac contractility, both of which may have increased in the study horses because of increased sympathetic activity in response to blood loss and dampened the decrease in CVP that was detected after removal of blood. These physiologic adaptations may also explain the increased variability (larger SD value) in the second CVP measurement made 30 minutes after removal of 16 mL of blood/kg because some of the horses may have begun to compensate with increased venous tone. However, despite the increased variability at this time point, the CVP remained significantly less than baseline value and also lower than the CVP value after replacement of 16 mL of blood/kg. Central venous pressure has long been suggested as an indicator of blood requirements after acute hemorrhage in humans.22 On the basis of our data, CVP appears to be more sensitive than heart rate or biochemical indices for detection of hypovolemia during early blood loss in horses. In fact, our findings suggest that negative CVP values in horses suspected of undergoing trauma indicate the presence of acute blood loss or hypovolemia. Without knowing baseline CVP values in individual horses in clinical situations, a CVP value that is within reference range (2 to 15 cm H2O) is difficult to interpret because hypovolemia may be present in the face of apparently normal CVP. However, in an equine patient that has recently undergone blood loss, negative CVP values should be considered indicative of hypovolemia. This is clinically relevant in that CVP values in the negative range can indicate early and potentially substantial blood loss (at least 16 mL/kg) in trauma patients, such as horses with lacerations involving blood vessels. Such values would warrant volume replacement as a minimum treatment and close monitoring to assess the need for blood transfusions.

Although heart rate increased slightly from baseline with removal of 16 mL of blood/kg in the horses of this report, this change was not significant. This is in contrast to the development of tachycardia detected in horses in a study by Weld et al23; however, those horses underwent removal of a greater volume of blood (10 to 15 L vs 7.4 to 9.3 L). Similar to the findings in our study, a lack of heart rate response to blood loss has also been reported for anesthetized horses and dogs, although the effects of inhalant anesthetics on baroreceptor responses in those species are unknown.24 A decrease in CVP with no change in heart rate (compared with baseline values) was also identified in a study25 performed to evaluate the effects of 500-mL blood loss in humans anesthetized for coronary bypass. In a study26 of acute hemorrhage in rabbits, there also
was a lack of tachycardia at the time CVP decreased. The fact that the horses of the present study did not develop tachycardia likely reflects the modest degree of blood loss, which may have been too mild to incite major baroreceptor and subsequent sympathetic responses. In addition, the small number of horses in our study may have been inadequate to detect a significant change in heart rate. These findings warrant further investigation of heart rate responses in conscious horses with acute hemorrhage.

Central venous pressure may also serve as an indicator of the end point for blood transfusions or volume restoration in horses with blood loss. When whole blood is administered as the replacement fluid in such patients, CVP is 1 indicator of the replenishment of blood volume. In the present study, CVP returned to baseline value with the restoration of blood volume. In clinical practice at present, it is difficult to identify when enough blood has been administered to a patient with acute hemorrhage, and a positive change in CVP (eg, an increase to ≥ 2 cm H2O from a negative value) may serve as 1 means of measuring transfusion adequacy. The catheter placement and technique for CVP measurement were straightforward, and there were no associated complications; therefore, this assessment should be feasible in clinical practice.

Blood lactate concentration was another reasonably useful indicator of early blood loss in horses. In response to reduced tissue oxygen delivery that accompanies hemorrhagic shock, blood lactate concentrations increase as a result of a relative increase in anaerobic glycolysis. In addition to hypovolemia and reduced oxygen content, blood loss may also result in hyperlactatemia associated with cardiovascular dysfunction such as myocardial or vasomotor dysfunction. Increased sympathetic activity, which might develop during acute blood loss, can also increase lactate production, as catecholamines lead to increases in tissue energy demand.25 According to results of the present study, blood lactate concentration > 1.1 mmol/L would be suggestive of blood loss in a horse with acute trauma involving major vessels. Blood lactate concentrations are expected to increase in proportion to the severity of blood loss. The lack of complete normalization of blood lactate concentration after blood transfusion in the horses of the present study may be related to the fact that it was measured immediately after completion of the transfusion, indicating some level of persistent abnormal tissue oxygen metabolism (dysoxia). Blood lactate concentration measurements performed later may have provided even lower values and a return to baseline values.

In human medicine, central venous oxygen saturation or oxygen tension is 1 indicator of the need for improved oxygen delivery.26 Increases in oxygen extraction ratio with reduced oxygen delivery (reduced cardiac output) result in lowered central venous oxygen tension, as can reduced arterial oxygen content, increased oxygen consumption, and altered distribution of peripheral blood flow. As a result of acute hemorrhage, venous oxygen saturation or tension would be expected to decrease in response to reduced oxygen delivery because of a decrease in cardiac output associated with hypovolemia and, possibly, altered myocardial function. In the present study, PcvO2 values decreased somewhat after blood loss but this difference was not significant. Perhaps with greater numbers of horses or more severe blood loss, this change in venous oxygen tension may have reached significance. These findings also suggest that blood lactate concentration and CVP may change earlier than PcvO2 values in response to blood loss in horses. The degree of blood removal in our study did not appear to substantially increase the oxygen extraction ratio (with resultant lowered PcvO2), as might be expected with larger volume losses. The potential decrease in PcvO2 in association with blood removal warrants further evaluation of central venous oxygen tension in horses with blood loss.

To the authors’ knowledge, this is the first study to evaluate acute blood loss in horses by use of hemodynamic indices applied to human patients, including CVP and blood lactate concentration. Results of our study suggest that these indices could be further studied as possible indicators of the need for blood transfusions in horses, rather than relying simply on heart rate and Hct. In addition, blood lactate concentration and CVP were apparently more sensitive than heart rate to the effects of blood removal. Therefore, changes in blood lactate concentration and CVP may be useful as early markers of acute hemorrhage in horses, whereas detection of tachycardia may be less reliable in states of mild to moderate blood loss. Alterations in CVP or blood lactate concentration may identify horses with blood loss that should be monitored closely for the need for transfusion.

References
Differences in hematocrit of blood samples obtained from two venipuncture sites in sharks
Natalie D. Mylniczenko et al

**Objective**—To evaluate differences in Hct between 2 venipuncture sites in captive and free-ranging sharks.

**Animals**—32 healthy adult captive sharks (Carcharhinus melanopterus, Carcharhinus plumbeus, Stegostoma fasciatum, Gonocephalus japonicus, and Triaenodon obesus) and 15 captured free-ranging adult sharks (Carcharhinus limbatus and Carcharhinus acronotus).

**Procedures**—Blood samples were collected from the caudal tail artery followed by collection from the sinus located immediately caudal to the cranial dorsal fin. The Hct was determined for each sample, and results were compared. Additionally, results for sharks that were highly active and used aerobic metabolism were compared with results for sharks that were less active and tolerant of anaerobic conditions.

**Results**—Mean Hct for all sharks was significantly less (8% less) in blood samples obtained from the cranial dorsal fin sinus, compared with the Hct for samples obtained from the caudal tail artery. When compared on the basis of metabolic class, sharks that were more tolerant of anaerobic conditions had lower Hct values and smaller differences between the 2 venipuncture sites.

**Conclusions and Clinical Relevance**—Hct values were significantly lower in blood samples collected from the cranial dorsal fin sinus, compared with values for samples collected from the caudal tail artery. It is important to recognize this difference when evaluating hematologic variables in sharks and when establishing reference ranges for Hct for shark populations. Sharks that were more active and relied on aerobic metabolism had higher Hct values than did anaerobic-tolerant sharks, and the difference in Hct values between venipuncture sites was more pronounced. (Am J Vet Res 2006;67: 699–702.)