Ultrasonographic Assessment of Caudal Vena Cava to Aorta Ratio as a Novel Endpoint in Hemorrhagic Shock Resuscitation in Dogs

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Abstract
Objective- The aim of this study was to assess ultrasonography-derived caudal vena cava to aorta ratio (CVC/Ao) as a novel endpoint in the resuscitation of experimental hemorrhagic shock in dogs.
Design- Experimental study.
Animals- Ten adult mongrel healthy dogs.
Procedures- After induction of anesthesia (control assessments), hemorrhagic shock was induced by blood withdrawal to a mean arterial pressure of 40 to 50 mmHg within 30 minutes and then maintained in a hypovolemic situation for an additional 30 minutes (second and third stages of assessments). Afterward, the dogs were randomly assigned to two groups which received 20 ml/kg lactated Ringer's solution or 5 ml/kg hydroxyethyl starch, in four consecutive 15 minutes intervals (fourth stage of assessments). One hour after the last resuscitation step, final ultrasonographic assessments were performed.
Results- Hemorrhagic shock caused a significant decrease in the CVC and Ao diameters as well as the CVC/Ao (2.14 ± 0.28 cm, 0.85 ± 0.07 cm and 0.4 ± 0.06, respectively) (p<0.05). Following the fluid resuscitation CVC/Ao increased and returned to pre-shock values in both groups.
Conclusion and clinical relevance- Findings indicated that serial ultrasonographic assessment of the CVC/Ao can be a useful endpoint in the resuscitation of dogs with hemorrhagic shock.

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1. Introduction

Hemorrhagic shock as the most common types of shock, is associated with morbidity and mortality in surgery and trauma patients. Intravenous fluids therapy is the cornerstone of managing patients with hemorrhagic shock. Reliable assessment of intravascular volume status during fluid resuscitation is crucial, because of either over- or under-resuscitation, can be perilous. When to stop fluid resuscitation would ideally be directed by universally established endpoints based on documented evidence. Unfortunately, such endpoints do not yet exist in veterinary medicine, and time to cessation of fluid therapy is often based on clinical parameters and laboratory data that can be challenging. Ultrasonography has garnered attention as a rapid, repeatable, and generally reliable method for assessment of fluid status, particularly in the care of patients in shock. Ultrasound may be used as an efficient tool in the identification of hypovolemia and to guide fluid management because it is safe, non-invasive, and applicable at the bedside. One of the routine ultrasonographic method that usually used to assess intravascular volume status in adult humans is measurement of the inferior vena cava (IVC) diameter and comparing it with reference values. But, in order to eliminate the problems arising from various body weight and size in pediatric patients a new ultrasonographic variable has been introduced recently. The inferior vena cava/aorta diameter is a useful variable for evaluation of intravascular volume that can predict fluid responsiveness in critical care patients. Similar to human subjects, there is also different dog sizes, therefore, use of an index of volemia such as those described for pediatric patients can be effective. Recent studies have shown that assessment of caudal vena cava to aorta ratio (CVC/Ao), as a marker of cardiac preload, is feasible method for estimation of hydration status in dogs. However, to our knowledge, assessment of CVC/Ao in the response to fluid therapy was not investigated previously. Therefore, the purpose of this study was to assess the CVC/Ao as a novel endpoint in the resuscitation phases of experimental induced hemorrhagic shock dogs with lactated Ringer’s solution or 6% hydroxyethyl starch.

2. Materials and Methods

Animals

Ten healthy male mongrel dogs, aged 1.5 to 3.5 years (weighing 18.56 ± 4.80 kg) were experimentally studied. Animals were determined to be in good health based on clinical and laboratory parameters and excluded if they had a relevant cardiac disease determined by the echocardiographic and electrocardiographic examinations. Food was withheld from each dog for 12 hours prior to experiment, but had free access to water. No splenectomy was performed in this study.

Animal preparation and instrumentation

After cannulation of left cephalic vein, with an 18-gauge catheter (for drugs and fluid administration), the anesthesia was induced with an intravenous bolus dose of propofol (Lipuro 1%, Braun, Melsungen, Germany) (6 mg/kg) and fentanyl (Caspian Tamin, Rasht, Iran) (5 µg/kg). Followed by intubation with an 8.0 to 8.5 mm cuffed endotracheal tube the animals were placed in left lateral recumbency and anesthesia was maintained with isoflurane (1.8%) in 100% oxygen. The left femoral artery was exposed by dissection and cannulated with a 16-gauge catheter, which was connected to a 3-way stopcock for induction of bleeding and to measure direct arterial blood pressure. Body temperature was maintained at 37° to 38°C with a heating blanket. Also, an experienced investigator evaluated physical parameters including mucous membrane color, capillary refill time and peripheral pulse quality routinely at the end of each step.
**Experimental protocol**

Ultrasonographic assessment of CVC/Ao was performed at the end of each step (A1 to A8) in five distinct stages as follows:

Control stage (A1): Baseline assessment was obtained after induction of anesthesia and instrumentation.

Hemorrhagic stage (A2): Each dog was then hemorrhaged to a mean arterial pressure (MAP) ranging from 40 to 50 mmHg. The procedure lasted approximately 30 min and blood was collected into sterile empty blood bags.

Hypovolemic stage (A3): The animals were left in shock situation for an additional 30 min period during which no fluid was administered. If a physiologic compensatory mechanism developed and MAP increased above the purpose values, more blood was removed to restore the MAP back to 40 to 50 mmHg.

Resuscitation stage (A4–A7): Animals were then randomly allocated into two equal groups. Group A was resuscitated with lactated Ringer's solution (LR) (Iranian Parenteral and Pharmaceutical Co., Tehran, Iran) at 20 ml/kg in 15 min for four consecutive times. Group B was resuscitated with 6% Hydroxyethyl Starch (HES) (Voluven, Fresenius Kabi, Homburg, Germany) at 5 ml/kg in a similar manner to group A.

Post-resuscitation stage (A8): The last assessment was performed one hour after termination of resuscitation. Then, animals were allowed to recover from anesthesia.

**Ultrasonographic technique**

Ultrasonographic assessment was performed using commercially available ultrasound machine (Landwind Medical, Model: Mirror 2, China) with a 5–7 MHz microconvex probe.

Our ultrasonographic technique has been described in detail previously by Meneghini and coworkers. In brief, the probe was located in a transverse position in the tenth to twelfth intercostal space (just few centimeters below to the spinal column), in order to find the porta hepatis. Upon visualization of the CVC and Ao, the image was frozen and cine loops were recorded. A single veterinary radiologist performed all ultrasonographic assessments and CVC/Ao calculations. All values were calculated three times, to minimize errors in measurements.

**Statistical analysis**

Data of this study were evaluated by repeated measures analysis of variance and LSD post hoc using SPSS 16.0 statistical software (SPSS, Inc., Chicago, USA). All data were presented as mean ± standard deviation (SD). A p value of less than 0.05 was considered as statistically significant.

**3. Results**

The average blood volume loss was 54 ± 4 ml/kg, which corresponded to approximately 62% ± 4% of the estimated circulating blood (88 ml/kg) volume; so that there were no significant differences between the groups (p>0.05). In both groups, the resuscitation were completed successfully with no mortality. There was no considerable difference between the studied groups according to MAP during all study stages (p>0.05). The mean time needed to ultrasonographic assessment after each step was 53 ± 10 seconds.

Hemorrhagic shock led to significant reduction in CVC and Ao diameters from 1.23 ± 0.08 and 2.36 ± 0.39 cm, respectively, in A1 to 0.85 ± 0.07 and 2.14 ± 0.28 cm, respectively, in A2 (p<0.05); that increased after fluids administration (Table 1).

The data in Figure 1 represent the CVC/Ao changes in the studied stages. The mean ± SD of CVC/Ao ratio in both groups before induction of shock was 0.53 ± 0.1, which was significantly reduced in A2 (0.04 ± 0.06) (p<0.05). Following the fluid therapy, this ratio increased and approximately returned to pre-shock values, at steps 4 and 7 in groups A and B, respectively. It is worth noting, the statistical analysis indicated no significant difference between solution types (p>0.05).
Table 1. Mean ± SD values of CVC and Ao diameters in dogs with experimental hemorrhagic shock after resuscitation with LR and HES.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Caudal vena cava diameter (cm)</th>
<th>Aorta diameter (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Steps</td>
<td>LR</td>
</tr>
<tr>
<td>A1</td>
<td>1.22 ± 0.07a</td>
<td>1.25 ± 0.08a</td>
</tr>
<tr>
<td>A2</td>
<td>0.85 ± 0.09a</td>
<td>0.85 ± 0.06a</td>
</tr>
<tr>
<td>A3</td>
<td>0.91 ± 0.09a</td>
<td>0.89 ± 0.05a</td>
</tr>
<tr>
<td>A4</td>
<td>1.16 ± 0.08a</td>
<td>0.99 ± 0.07a</td>
</tr>
<tr>
<td>A5</td>
<td>1.23 ± 0.07a</td>
<td>1.05 ± 0.06a</td>
</tr>
<tr>
<td>A6</td>
<td>1.29 ± 0.06a</td>
<td>1.13 ± 0.07b</td>
</tr>
<tr>
<td>A7</td>
<td>1.35 ± 0.04a</td>
<td>1.26 ± 0.08a</td>
</tr>
<tr>
<td>A8</td>
<td>1.24 ± 0.04a</td>
<td>1.3 ± 0.07a</td>
</tr>
</tbody>
</table>

Note: Different lowercase in each column denote significant differences (p<0.05).

Figure 1. Mean ± SD values of CVC/AO in dogs with experimental hemorrhagic shock after resuscitation with LR and HES.

4. Discussion

In this study, after induction of severe hemorrhagic shock, animals were resuscitated with LR and HES as the most frequently used crystalloid and synthetic colloid fluids in veterinary medicine.

The endpoint of resuscitation occurs when a patient has been fluid resuscitated adequately. Traditionally, resuscitation endpoints including restoration of normal clinical perfusion parameters (i.e., heart rate, capillary refill time, peripheral pulse quality, and rectal temperature), blood pressure, and urine output remain the standard of care. However, reliance on these traditional endpoints of resuscitation, due to body's compensatory mechanisms for initial volume loss, may not provide a reliable enough estimate of volume status and occult shock can occur eventually. For example, blood pressure measurement, as the main marker in evaluating emergency situations, is often used to gauge the adequacy of resuscitation. Interestingly, Wo et al. demonstrated that blood pressure is an unreliable indicator of acute blood loss and accordingly is poor marker of the severity of the shock as well as response to treatment.

The CVC-to-Ao ratio have been demonstrated to be strongly correlated with hemodynamic parameters and the CVC diameter has been proposed to reflect volume status more closely than other variables based on the arterial system, such as blood pressure, pulse rate or quality, and Ao diameter. Furthermore, Akilli et al. proved that ultrasonographic measurement of the IVC diameter, as a marker of early hemorrhagic shock, is more accurate than the shock index and other routinely used non-invasive predictors of acute blood loss such as heart rate, serum lactate level, and base deficit. In another study, IVC diameter strongly reflect the central venous pressure which is currently considered the most precise method in assessing patients' fluid status.

In our study, as expected, hypovolemia caused by hemorrhagic shock led to decrease in CVC diameter. However, in contrast to the recent study by Cambournac et al., Ao diameter also showed a significant decrease after blood loss which can be attributed to severe hypovolemia, than milder one that was reported. As intravenous fluids were administered, the CVC diameter increased a little more than the aorta. This may be due to differences in vessel characteristics. Histologically, the CVC has a thinner wall than the aorta, with less defined layers, as well as decreased number of smooth myocytes. In addition, veins have less elasticity than arteries. The venous system acts as a fluid reservoir that contains 65–75% of total blood volume, with the most contribution created by splanchnic venous system.

In light of the mentioned issues, assessment of CVC/Ao may be a reasonable method to monitor the response to fluid resuscitation. In our experiment, significantly
hypovolemic dogs showed a decrease in mean value of CVC/Ao, that was lower than the results of another study that evaluate CVC/Ao after a blood donation of 9.8 ± 2.2 mL/kg (0.4 versus 1.01). The CVC/Ao increased slightly after fluid resuscitation and almost returned to control values that can indicate successful resuscitation in both groups. In normovolemic dogs that were admitted for surgical repair of skin wounds, the mean value of CVC/Ao after bolus administration of Hartmann solution (14 ± 7 mL/kg) was 0.91 that was higher than our results. The difference in the results may be associated with the differences in anesthetic protocols, intravascular volume status, fluid therapy methods, and ultrasonographic techniques.

The lack of significant difference in CVC/Ao values between the two types of solutions that were used, despite different dosage, probably is due to the discrepancy in mechanisms of action as well as the stability time in the vessels of infused fluids.

Ultrasonographic assessment of CVC/Ao to guide fluid resuscitation also makes it possible to assess abdominal (liver, spleen, kidneys) and thoracic organs (heart, lungs) in daily practice. However, Ultrasound has some disadvantages. The results are operator dependent, and the image quality is affected by anatomical obstacles such as large fat deposits and excessive abdominal gas. According to Tan et al. study, some situations including right ventricular dysfunction, tricuspid valve disease, liver cirrhosis, tension pneumothorax, asthma, pericardial tamponade, increasing age, and ethnicity of patients can affect the IVC diameter and making it less reliable.

There were some limitations in our study. Firstly, the dogs were under anesthesia and it alters hemodynamic variables by reducing cardiac contractility, vascular tonic, and changing cardiovascular responses to variation in blood pressure and volume. However, in the study reported here, anesthesia was maintained using isoflurane to restrict potential confounding hemodynamic effects. Secondly, the animal position may affect the CVC diameter.

Although not investigated in dogs, but it is demonstrated that the position of the human patients can influence IVC diameter. So that, left lateral recumbency making the smallest diameter and right lateral recumbency making the largest IVC diameter. Finally, ultrasonographic assessments were performed by a single operator and involving more operators could improve the validity of the results.

In conclusion, ultrasonographic assessment of CVC/Ao can provide an affordable and simple method for estimation the resuscitation endpoint beside a comprehensive physical examination in dogs with hemorrhagic shock. Further studies are now needed to establish reference intervals for CVC/Ao, in order to guide the resuscitation of referral dogs in daily practice that have uncertain pre-shock values.

Acknowledgment

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Conflict of interest

The authors declare no conflict of interest.

References


چکیده

ارزیابی اولتراسونوگرافی نسبت بزرگ سیاه‌رگ پسین به آئورت به عنوان نقطه جدید در احیای شوک هموارازیک در سگ

چهارگروه 1، رضا آویزه 2، علیرضا غدیری 3، هادی ایمانی راستابی 4، مهدی پورمهدی 5

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هدف - هدف از این مطالعه ارزیابی اولتراسونوگرافی نسبت بزرگ سیاه‌رگ پسین به آئورت به عنوان یک نقطه جدید در خانه احیای سگ‌های دچار شوک هموارازیک است.

طرح مطالعه - طرح‌خوانی تجريبي.

حيوانات - د، انگل سگ بالغ سالم آنها در مرحله دوم و سوم.

روش کار - پس از این مطالعه ارزیابی اولتراسونوگرافی نسبت بزرگ سیاهرگ پسین به آئورت به عنوان نقطه جدید در احیای سگ‌ها، با توجه به هدف از این مطالعه، به آگاهی از ارزیابی اولتراسونوگرافی نسبت بزرگ سیاهرگ پسین به آئورت در شوک هموارازیک باشد.

نتایج - نتایج پایانی مفید در احیای سگ‌های دچار شوک هموارازیک باشد.