Fluid Therapy in Equine Patients: Small-Volume Fluid Resuscitation

Lucas G. Pantaleon, DVM, MS, DACVIM
Woodford Equine Hospital
Versailles, Kentucky

Abstract: Fluid therapy is an important component of resuscitation and treatment of critically ill equine patients. However, the decision of which fluid type to use in certain critical situations is somewhat controversial. This article focuses on the potential benefits of performing small-volume resuscitation in critically ill horses by combining hypertonic saline with a colloid (e.g., hetastarch).

In horses and humans, the optimal fluid for resuscitation varies according to the clinical situation. However, the goal of fluid therapy is always to maintain vascular volume, blood pressure, and cardiac output to prevent organ dysfunction.

Fluid therapy is essential to decrease mortality and accelerate recovery. An adequate fluid therapy plan requires evaluation of the patient's physical condition, understanding of the principles of body fluid homeostasis and distribution, and selection of the appropriate fluid type.

The major questions regarding fluid therapy in critically ill equine patients are the following:

- Which fluids or fluid combinations should be used?
- Which regimen is safest and most effective?

The goals of fluid therapy resuscitation in critically ill patients (e.g., those with hypovolemia and septic shock) include correction of hypotension and hypovolemia to achieve the following:

- Stabilize the cardiovascular system and improve cardiac output (e.g., blood pressure, capillary refill time, distal limb perfusion)
- Improve organ perfusion (e.g., mentation, urine output) and normalize tissue oxygenation
- Correct electrolyte and acid–base abnormalities (e.g., lactate concentration)
- Stabilize vital signs (e.g., temperature, pulse, respiration)

In equine patients, fluid therapy is the mainstay for treating conditions such as sepsis, endotoxemia, colic, hypovolemia, and shock. Shock can be initiated by diverse etiologies and is characterized by failure of the circulatory system to maintain tissue perfusion, ultimately resulting in irreversible cellular damage if not corrected. Distributive shock, which is caused by sepsis or endotoxemia, is a more complex form of shock characterized by peripheral vasodilation despite preserved or increased cardiac output, leading to ineffective tissue oxygen delivery and extraction. Furthermore, deleterious effects of systemic inflammatory response syndrome (SIRS) on endothelial cells result in hypovolemia despite adequate fluid therapy. During SIRS, vascular damage with secondary edema formation occurs, and uncontrolled neutrophil activation induces tissue damage. Moreover, activation of coagulation and fibrinolysis leads to disseminated intravascular coagulation. These events ultimately result in organ dysfunction and failure.

Key Points

- Prevention of multiple organ dysfunction or failure is the ultimate goal of fluid resuscitation.
- Plasma volume expansion using a hydroxyethyl starch solution can be equivalent to the volume infused.
- Rapid correction of hemodynamics and ease of transport make small-volume resuscitation an attractive therapy. However, after this therapy, it is imperative to quickly administer crystalloid fluids to maintain vascular volume and interstitial and cellular fluid levels.
- In this article, small-volume resuscitation refers to rapid infusion of a combination of hypertonic saline and hetastarch, a colloid.
Fluid Therapy in Equine Patients

Types of Fluid Therapy

The electrolyte compositions of commercial crystalloid and colloid preparations are summarized in Table 1. Crystalloids (i.e., Normosol-R [Abbott Laboratories], lactated Ringer’s solution, 0.9% NaCl) are the most widely used resuscitation fluids in equine patients and can also be classified as maintenance fluids.11,12 The typical administration rate for crystalloids during fluid resuscitation is 60 to 80 mL/kg as a bolus. However, the use of a large volume of 0.9% NaCl has been associated with hyperchloremic metabolic acidosis due to an increased plasma chloride concentration and a decreased strong ion difference.13,14 Hypertonic saline solution is a hyperosmotic crystalloid with a high sodium content (7.2% to 7.5%). It is primarily used for small-volume resuscitation (defined as rapid infusion of hypertonic saline [3 to 6 mL/kg] with or without colloids).15–17 In this article, small-volume resuscitation refers to the rapid infusion of a combination of hypertonic saline and hetastarch, a colloid.

Maintenance crystalloids contain a higher potassium concentration and lower sodium and chloride concentrations than resuscitation crystalloids. Crystalloids are administered at a maintenance rate after resuscitation fluid therapy. The typical maintenance rate is 2.5 mL/kg/h for adult horses and 3 to 5 mL/kg/h for neonatal foals.18

Colloids can be natural (plasma, whole blood) or synthetic (hydroxyethyl starch solutions [hetastarch, pentastarch], dextran, polymerized hemoglobin).9 When crystalloids and colloids are titrated to the same level of filling pressure, they are equally effective in restoring tissue perfusion.4,9,19,20 Hydroxyethyl starch solutions are the focus of this article.

The goals of fluid resuscitation are listed in Table 2.

Hydroxyethyl Starch

Hydroxyethyl starches are synthetic polymers derived from amylopectin, a branched polysaccharide polymer.21,22 Hydroxyethyl starches are polydisperse colloids, meaning they contain a range of different molecular-weight particles.21,22 The pharmacokinetics of a hydroxyethyl starch are related to its size (molecular weight), which determines colloidal activity, and its degree of substitution (attachment of hydroxyethyl ether groups to carbons 2, 3, and 6 of the glucose moieties).21,22,24,25 The degree of substitution determines metabolism (by serum amylase) and circulating half-life; thus, the higher the degree of substitution (expressed by a number between 0 and 1), the slower the metabolism, and the longer the duration of effect.21,22 The many types of hydroxyethyl starch differ in their concentration, molecular weight, and degree of substitution. In the United States, two types of hydroxyethyl starch with a high average molecular weight (670 kD) and degree of substitution (0.7 to 0.75 [70% to 75% of starch molecules carry a hydroxyethyl group]) are approved for volume expansion (i.e., 6% hetastarch in 0.9% NaCl; 6% hetastarch in lactated balanced electrolyte solution).13,25

When hydroxyethyl starch is administered, particles smaller than 50 kD are rapidly eliminated by glomerular filtration.6,21,22 Larger particles are hydrolyzed by serum amylase and then excreted mostly in urine.21,22 In equine patients, one-third of the volume of hydroxyethyl starch infused is found in urine within 24 hours, making the kidneys the main route of elimination.26 Another mechanism of elimination is uptake by the reticuloendothelial system.22 In healthy horses, the oncotic effects of infused hydroxyethyl starch (volume expansion) last for approximately 24 hours; in ill horses, the duration of these effects may be greatly reduced by increased vascular permeability.24,27

Synthetic colloids composed of large molecules increase plasma colloid oncotic pressure (e.g., administration of 1 L of hydroxyethyl starch solution results in 700 mL to 1 L of plasma

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**TABLE 1**  Types and Electrolyte Composition of Selected Fluid Solutions

<table>
<thead>
<tr>
<th>Crystalloids</th>
<th>Solution</th>
<th>Na⁺ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Ca** (mEq/L)</th>
<th>Mg** (mEq/L)</th>
<th>Osmolality (mOsm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resuscitation and maintenance</td>
<td>Normosol-R (Abbott Laboratories)</td>
<td>140</td>
<td>98</td>
<td>5</td>
<td>—</td>
<td>3</td>
<td>294</td>
</tr>
<tr>
<td></td>
<td>Lactated Ringer’s solution</td>
<td>130</td>
<td>109</td>
<td>4</td>
<td>3</td>
<td>—</td>
<td>273</td>
</tr>
<tr>
<td></td>
<td>0.9% NaCl</td>
<td>154</td>
<td>154</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>308</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>Hypertonic saline 7.2%</td>
<td>1232</td>
<td>1232</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2464</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Normosol-M (Abbott Laboratories) and 5% dextrose</td>
<td>40</td>
<td>40</td>
<td>13</td>
<td>—</td>
<td>3</td>
<td>363</td>
</tr>
<tr>
<td></td>
<td>Plasma-Lyte 56 (Baxter) and 5% dextrose</td>
<td>40</td>
<td>40</td>
<td>13</td>
<td>—</td>
<td>3</td>
<td>363</td>
</tr>
<tr>
<td>Colloids</td>
<td>Synthetic</td>
<td>Hetastarch (Hospira)</td>
<td>154</td>
<td>154</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Hextend (Hospira)</td>
<td>143</td>
<td>124</td>
<td>3</td>
<td>5</td>
<td>0.9</td>
<td>307</td>
</tr>
</tbody>
</table>
Sepsis and endotoxemia cause SIRS, in addition, hypertonic saline reduces expression of adhesion molecules. 

In a prospective, randomized clinical trial involving 30 horses that required colic surgery, improved global perfusion was observed when hydroxyethyl starch was used before colic surgery compared with horses that received hypertonic saline; the improvement was noted for 150 minutes after induction of anesthesia. Compared with crystalloids, hydroxyethyl starch administered to humans undergoing abdominal surgery improved tissue oxygenation, likely by improving microcirculation. In a septic shock porcine model, plasma volume was maintained in hydroxyethyl starch–resuscitated animals, suggesting persistence of colloids during capillary leakage.

**Hypertonic Saline Solution**

Hypertonic saline resuscitation is suggested as a valuable alternative to traditional fluid regimens in treating different types of shock. Hypertonic saline increases intravascular volume by mobilizing endogenous fluids along an osmotic gradient from the interstitium, endothelial cells, and erythrocytes. Furthermore, the hypertonicity induced by hypertonic saline causes arteriolar vasodilation, reducing systemic vascular resistance. Ultimately, tissue perfusion and cardiac output are improved. Hemodynamic improvements such as increased cardiac output and stroke volume, which peak at 20 minutes after infusion and decline thereafter, were observed in horses with experimentally induced hemorrhagic and endotoxic shock treated with hypertonic saline.

In addition, hypertonic saline reduces expression of adhesion molecules in leukocytes and endothelial cells, limiting their interaction and preventing endothelial damage (leakage). Antiinflammatory effects of hypertonic saline result in reduced tissue damage and organ failure. Therefore, the beneficial effect of hypertonic saline in septic shock is twofold: hemodynamic and antiinflammatory.

**Small-Volume Resuscitation**

In this article, small-volume resuscitation is defined as the rapid infusion of a combination of hypertonic saline and a colloid (hetastarch). For each milliliter of hypertonic saline infused, plasma volume increases by 3 mL; this is the basis of small-volume resuscitation. However, this effect is short lived; thus, to sustain the hemodynamic effects of hypertonic saline, it is used in combination with a colloid. There is a synergistic effect in combining hypertonic saline, which increases plasma osmolality and mobilizes intracellular water, with a colloid, which increases plasma oncotic pressure, conserving the volume effect. Based on this principle, I combine hypertonic saline (5 mL/kg) with hetastarch (5 to 10 mL/kg) for small-volume resuscitation (as a bolus over 20 minutes, depending on the volume). After small-volume resuscitation, it is imperative to quickly administer crystalloid fluids to maintain vascular volume and interstitial and cellular fluid levels.

**Complications of Fluid Therapy**

The major complications of fluid resuscitation are pulmonary and interstitial edema. Three factors contribute to edema formation: increased hydrostatic pressure, decreased colloid oncotic pressure, and increased microvascular permeability associated with sepsis. Colloid advocates argue that crystalloids leak from plasma, excessively expanding intrastitial fluid volume, whereas crystalloid supporters argue that colloid leakage into the interstitial space contributes to edema. Ultimately, edema is deleterious because it affects organ function by interfering with oxygen exchange. Furthermore, fluid leakage causes decreased intravascular

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**TABLE 2 Fluid Resuscitation Goals in Neonates and Adults**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Goals in Neonates</th>
<th>Goals in Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillary refill time (sec)</td>
<td>&lt;2</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>&gt;69</td>
<td>&gt;65</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>&lt;2.5</td>
<td>&lt;2</td>
</tr>
<tr>
<td>S&lt;sub&gt;0&lt;/sub&gt; (%)</td>
<td>&gt;75</td>
<td>&gt;75</td>
</tr>
<tr>
<td>Central venous pressure (cm H&lt;sub&gt;2&lt;/sub&gt;O)</td>
<td>2–9</td>
<td>7.5–12</td>
</tr>
<tr>
<td>Urine output (mL/kg/h)</td>
<td>Output ≥66% of input</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Rectal temperature (°F)</td>
<td>99–102</td>
<td>99–101</td>
</tr>
<tr>
<td>Extremities</td>
<td>Warm</td>
<td>Warm</td>
</tr>
</tbody>
</table>
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volume, negatively affecting cardiac output and tissue perfusion. The use of crystalloids and colloids is accompanied by peripheral edema.19 Studies in humans have failed to demonstrate overall differences in mortality, pulmonary edema, or length of hospitalization among various fluid therapies.1,4,19 In ideal conditions, only 21% to 25% of the infused crystalloid remains in the intravascular space, while in septic patients, merely 100 to 200 mL of volume expansion can be anticipated after infusion of 1 L of isotonic crystalloids.4,6,37

Resuscitation with crystalloids requires the use of much larger volumes than those used for colloids (i.e., 80 mL/kg of crystalloid fluid for resuscitation of equine patients in endotoxic shock), which causes hemodilution and decreases colloid oncotic pressure.2,4,6,10 Administration of such a large volume of fluid to a critically ill patient with already-compromised (“leaky”) vasculature may potentiate interstitial and pulmonary edema, affecting tissue oxygenation and organ function. Volume overload, assessed by marked elevation in central venous pressure (CVP), was observed in endotoxemic horses resuscitated with a large volume of crystalloids (60 mL/kg; FIGURE 1).38

Dose-dependent alterations in von Willebrand’s factor and factor VIII were observed in normal ponies treated with 10 or 20 mL/kg of hetastarch.10 However, these alterations were not severe enough to prolong clotting parameters.10 In vitro hydroxyethyl starch in a balanced electrolyte solution (Hextend, Hospira) had minimal adverse effects on coagulation compared with hetastarch.41 Therefore, hydroxyethyl starch preparation might be an important factor to consider when choosing the type of solution to use.

In an in vitro study, hypertonic saline was shown to have antiplatelet and anticoagulant effects.42 Another risk of using hypertonic saline is induction of a hypertonic state due to sodium overload.4,9

Small-volume resuscitation (5 mL/kg of hypertonic saline followed by 10 mL/kg of hetastarch) in anesthetized horses with induced endotoxic shock did not have deleterious effects on coagulation compared with large-volume resuscitation or no resuscitation.43

Small-Volume Resuscitation in the Clinical Setting

In adult horses, endotoxemia commonly originates secondary to gastrointestinal disease (i.e., colitis) due to endotoxin translocation through an inflamed gut wall.41 In pigs with experimentally induced endotoxic shock, small-volume resuscitation (hypertonic saline plus dextran) effectively prevented microcirculatory and metabolic deterioration of the intestinal mucosa, ultimately improving survival.17 To my
knowledge, the effect of small-volume resuscitation on the equine gut has not been studied. In a severe equine endotoxin model in which 50 µg/kg of Escherichia coli endotoxin was infused intravenously in anesthetized adult horses, small-volume resuscitation (5 mL/kg of hypertonic saline and 10 mL/kg of hetastarch) supported preload without volume overload. \(^3^8\) I use small-volume resuscitation without exceeding the above-mentioned dosages (as a bolus over ~20 minutes, depending on the volume) in adult horses presenting with severe hypovolemic or endotoxic/septic shock (i.e., severe enterocolitis). This is followed by constant-rate infusion of isotonic crystalloids and supplementation of necessary electrolytes. Most of these horses respond positively to small-volume resuscitation. The rationale behind using small-volume resuscitation in endotoxic horses is multifactorial (e.g., avoidance of volume overload, sealing of leaky vessels, antiinflammatory effects).

Colic is a major cause of morbidity and mortality in horses, and any delay in surgery can negatively affect patient outcome, particularly in patients with strangulated lesions. \(^2^7\-^4^5\) Furthermore, in extremely painful patients, the fluid volume that can be given before anesthesia is limited. Therefore, the ease of transport, rapid administration, and rapid correction of hemodynamics characteristic of small-volume resuscitation could be especially useful for resuscitating equine patients with severe abdominal pain before anesthesia, if crystalloid fluids can be administered immediately after small-volume resuscitation. Therefore, rapid resuscitation and cardiovascular stabilization with small-volume resuscitation could have a positive effect on horses with abdominal pain. Moreover, the time necessary to adequately resuscitate an adult horse using isotonic crystalloids could negatively affect outcome, especially in patients with a strangulating lesion. Horses with severe abdominal pain and signs of hypovolemic shock that are admitted to my hospital are treated with small-volume resuscitation before surgical intervention. My clinical assessment is that these horses are hemodynamically more stable during surgery, which may improve their outcome.

Hemorrhagic shock is another critical situation in which rapid correction of hemodynamics could positively affect outcome. Horses with experimentally induced hemorrhagic shock treated with hypertonic saline (3.8 to 4.5 mg/kg) had temporary but significant improvement in cardiac output and mean arterial pressure along with decreased systemic vascular resistance. \(^3^2\) There is concern that this effect could overwhelm hemostatic mechanisms, making the use of small-volume resuscitation a risk for further bleeding. \(^3^4\) However, at least in humans, small-volume resuscitation during penetrating trauma or complex cardiovascular surgery (in which hemostatic alterations are common) has been associated with decreased fluid requirements, no increase in transfusion, and decreased morbidity and mortality. \(^3^4\) These data suggest there is no increased bleeding associated with small-volume resuscitation. \(^3^4\) However, more research in horses is needed to validate this; small-volume resuscitation in patients with severe hemorrhagic shock must be carefully evaluated by clinicians; and the benefits of this therapy must be carefully balanced with potential risks on a case-by-case basis. Moreover, therapy for hemorrhagic shock could depend on the form of hemorrhage (i.e., uncontrolled [e.g., intraabdominal, uterine artery rupture, pulmonary hemorrhage] versus controlled hemorrhage). \(^4^6\)

**Conclusion**

Small-volume resuscitation has several valuable properties, making it attractive for use in critically ill patients, if crystalloid fluids can be administered immediately afterward. Despite these benefits, more studies are needed to elucidate the effects of this therapy on morbidity and mortality, and it is important to consider the potential deleterious effects of...
this therapy on hemostasis. To minimize these effects, the dose should not exceed 10 mL/kg (e.g., not exceeding 5 L for a 500-kg horse) for hydroxyethyl starches or 5 mL/kg (e.g., not exceeding 2.5 L for a 500-kg horse) for hypertonic saline (as a bolus over ~20 minutes, depending on the volume). If the patient has an evident coagulopathy (e.g., prolonged bleeding or hematoma after venipuncture, thrombophlebitis, epistaxis, petechiae, ecchymosis), diligent evaluation of the clinical situation is recommended before administration of small-volume resuscitation.

Research is ongoing, with the aim of better understanding which fluid therapy protocol is most appropriate in specific clinical situations. Until further investigation elucidates this issue, the fluid therapy protocol depends on the clinical situation, the veterinarian’s preference, and the cost.

References
1. Why does large-volume infusion of 0.9% NaCl for resuscitation cause metabolic acidosis?
   a. It increases the plasma chloride concentration.
   b. It decreases the plasma chloride concentration.
   c. It increases the strong ion difference.
   d. It decreases the plasma sodium concentration.
   e. none of the above

2. What is one difference between resuscitation and maintenance crystalloids?
   a. Resuscitation fluids contain higher concentrations of potassium and chloride.
   b. Resuscitation fluids contain a lower potassium concentration.
   c. Resuscitation fluids contain a lower sodium concentration.
   d. Resuscitation fluids contain a lower chloride concentration.
   e. Resuscitation fluids contain higher concentrations of potassium and sodium.

3. For a hydroxyethyl starch solution, a degree of substitution equal to 1
   a. indicates that the duration of effect is very short.
   b. indicates that the solution would be rapidly metabolized.
   c. is very low.
   d. indicates that the metabolism is slow and the duration of effect is long.
   e. indicates nothing regarding metabolism of the solution.

4. Which statement regarding hydroxyethyl starch molecules is correct?
   a. High-molecular-weight molecules could seal endothelial gaps.
   b. Their molecular weight has no influence in sealing endothelial gaps.
   c. Very low–molecular-weight (<50 kD) molecules could seal endothelial gaps.
   d. Medium-molecular-weight (100 to 300 kD) molecules could seal endothelial gaps.
   e. The higher the degree of substitution, the more endothelial pores are sealed.

5. Which statement regarding the effects of hydroxyethyl starch solution on coagulation is correct?
   a. Easily degradable hydroxyethyl starch solutions have the most deleterious effect on coagulation.
   b. The dosage of hydroxyethyl starch solutions does not appear to affect coagulation.
   c. Medium- or low-molecular-weight hydroxyethyl starch solutions are believed to exert the least deleterious effects on coagulation.
   d. Platelet function is enhanced by hydroxyethyl starch solutions.
   e. To decrease the risk of adverse effects on coagulation, solutions with a hydroxyethyl starch concentration >20 mL/kg are recommended.

6. By which mechanism do hypertonic saline solutions increase intravascular volume?
   a. by providing a large volume of hypertonic saline
   b. by mobilizing endogenous fluids
   c. by stimulating thirst
   d. by increasing tissue edema formation
   e. none of the above

7. How is small-volume resuscitation defined in this article?
   a. small-volume infusion of an isotonic crystalloid
   b. small-volume infusion of a hypotonic crystalloid
   c. rapid infusion of an isotonic crystalloid and a colloid
   d. rapid infusion of hypertonic saline and a colloid
   e. constant-rate infusion of a hypertonic saline solution

8. What is the main advantage of small-volume resuscitation?
   a. decreased mortality and morbidity
   b. slow correction of hemodynamics
   c. administration by slow infusion
   d. rapid administration and rapid correction of hemodynamics
   e. none of the above

9. What is the ultimate goal of fluid resuscitation in critically ill equine patients?
   a. prevention of peripheral edema
   b. increased urinary production
   c. correction of the serum potassium concentration
   d. prevention of multiple organ dysfunction or failure
   e. increased CVP

10. What is the major complication of fluid resuscitation in critically ill patients?
    a. venous thrombosis
    b. tissue edema
    c. bacteremia
    d. air embolism
    e. electrolyte imbalances