Hypertonic Saline Solutions in Shock Resuscitation

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Abstract: *Hypertonic saline solutions (HSS) have several characteristics that may improve the survival of patients during the initial treatment of certain types of shock. The use of isotonic crystalloids for resuscitation has several limitations: large infusion volumes are needed to increase the intravascular space; these large volumes cannot be given rapidly; and the fluid rapidly redistributes throughout the extravascular space. HSS are administered as a small-volume bolus over a few minutes and, by mobilizing extravascular water to the intravascular space, result in an immediate restoration of intravascular volume that can last several hours. Additional properties of HSS include positive effects on cardiac function, the microvasculature, and the immune system that not only justify their use in shock resuscitation but also suggest the opportunity for other applications.*

The ideal resuscitative fluid for hypovolemic shock would expand intravascular volume and improve mean arterial pressure (MAP), cardiac output (CO), and perfusion. Additionally, this fluid would be effective at a small infusion volume that could be administered rapidly, and the cardiovascular effects would be sustained for several hours after the initial infusion. Finally, it would be safe to administer to any patient without causing complications.

Hypertonic saline solutions (HSS) are crystalloid solutions with concentrations of sodium and chloride and an osmolarity exceeding those of normal plasma[1–4] (**TABLE 1**). Unlike some other crystalloid solutions, such as Normosol

R, lactated Ringer solution, and Plasmalyte, HSS contain no potassium, calcium, magnesium, dextrose, or buffers and have no effect on colloid osmotic pressure. HSS are available in 7%, 7.2%, 7.5%, and 23% NaCl solutions; unless otherwise specified, this article refers to 7% HSS.

Physiologic Effects
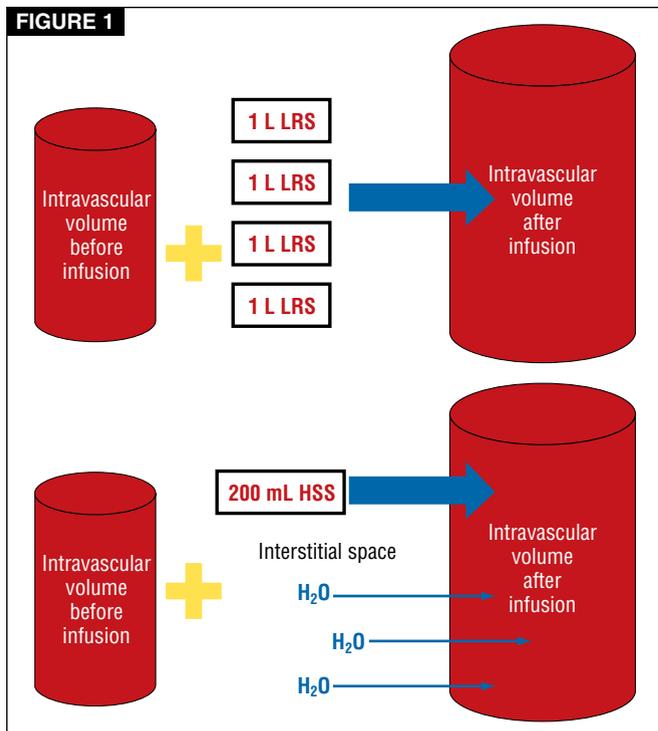
Intravascular Volume Expansion

HSS are unique among crystalloid solutions in their ability to provide immediate intravascular volume expansion with small infusion volumes. This volume expansion is primarily due to their high sodium concentration, which increases plasma osmolarity. The higher osmolarity results in the immediate movement of water from the interstitial space into the intravascular space. Subsequently, the interstitial sodium concentration increases, causing water to move from the intracellular compartment into the interstitium until equilibrium is reached.[5] The resultant intravascular volume expansion is in excess of the infused volume, which can be ideal in

TABLE 1 Physical Properties of Various Saline Solutions Relative to Plasma[1–4]

Solution	Sodium (mEq/L)	Chloride (mEq/L)	Osmolarity (mOsm/L)	Colloid Osmotic Pressure (mm Hg)
0.9% NaCl	154	154	308	0
3% NaCl	510	510	1030	0
5% NaCl	856	856	1711	0
7% NaCl	1283	1283	2566	0
7% NaCl/6% dextran 70	1285	1285	2566	75
Plasma	145	105	300	18–24

NaCl = sodium chloride.

FIGURE 1

Comparison of infused fluid volumes necessary to achieve similar expansion of intravascular volume. *HSS* = hypertonic saline solution; *LRS* = lactated Ringer solution.

clinical situations (e.g., head trauma, pancreatitis, burns) in which large fluid volumes may promote detrimental interstitial edema. **FIGURE 1** compares the plasma volume expansion after the infusion of HSS and isotonic crystalloids.

Several studies have attempted to quantify the degree of plasma volume expansion after the administration of HSS.[6–10]

TABLE 2 **Studies Evaluating Plasma Volume Expansion in Patients With Hemorrhagic Shock**

Author	Fluid Type	Dose (mL/kg)	Duration of Infusion (min)	Plasma Volume Expansion (mL/kg) Over Time[a]		
				0 min	60 min	180 min
Velasco et al[6]	HSS	4	10		5	
Smith et al[7,b]	HSS	4	2	10		3
	HSD	4	2	15		10
Velasco et al[8]	HSS	6	2	21		5
	HSD	6	2	26		14
Schertel et al[9]	HSS	8	5	15		

[a]Not all studies evaluated plasma volume expansion at the same time intervals.
[b]Data were extrapolated from Figure 5 of the cited study because the specific numbers were not available.
HSD = hypertonic saline solution combined with 6% dextran 70, *HSS* = hypertonic saline solution.

Most of these studies involved inducing hypovolemic shock by controlled hemorrhage equivalent to 30% to 40% of the total blood volume, administering a single bolus of HSS or HSS combined with 6% dextran 70 (HSD), and monitoring the plasma volume expansion. As shown in **TABLE 2**, plasma volume expansion with HSS was highest immediately postinfusion (0 min) and then quickly equilibrated with the extracellular fluid compartment to result in minimal expansion 1 to 3 hours later. The use of HSD resulted in the greatest initial plasma volume expansion, which persisted 3 hours later. This is one reason to consider combining HSS with colloids for immediate and sustained plasma volume expansion, respectively.

Studies[6,10] that evaluated plasma volume expansion in normovolemic dogs found that the administration of 0.9% saline solution resulted in the highest initial plasma volume expansion (**TABLE 3**); this was attributed to the fact that saline solution had the largest infusion volume relative to the other fluids. Silverstein and colleagues[10] calculated efficiency ratios to represent the change in plasma volume relative to the volume infused and found that HSS resulted in the greatest plasma volume expansion 30 minutes postinfusion, with an efficiency ratio two- to threefold greater than any of the other solutions immediately postinfusion. They concluded that HSS had the highest blood volume expansion—almost three times the volume infused—because of the recruitment of fluid from other compartments into the vascular space. The volume-expanding effects of HSS were short-lived but lasted at least 30 minutes, whereas the synthetic colloids had significant plasma volume expansion at 240 minutes.[10] These studies demonstrate that in normovolemic and hypovolemic patients, infusions of HSS lead to an immediate plasma volume expansion greater than the volume infused. The effect of HSS alone on plasma volume expansion lasts only 1 to 3 hours. The plasma volume expansion appears to be dose related, as a 6-mL/kg dose resulted in greater volume expansion than a 4-mL/kg dose.

Cardiovascular Effects

The use of small-volume HSS infusions in patients with hypovolemic shock has been shown to rapidly improve cardiovascular function as immediate volume expansion results in increased CO, MAP, contractility, and venous return and reduced peripheral vascular resistance (PVR).[8,11,12]

In a feline model of hemorrhagic shock, a 4-mL/kg infusion of HSS increased MAP and CO for 15 to 55 minutes. This study also measured levels of myocardial depressant factor (MDF), which has negative inotropic effects and constricts splanchnic vasculature. MDF levels were

TABLE 3 **Studies Evaluating Plasma Volume Expansion in Normovolemic and Normotensive Patients**

Author	Fluid Type	Dose (mL/kg)	Duration of Infusion (min)	Plasma Volume Expansion (mL/kg) Over Time (Efficiency Ratio)[a]				
				0 min	10 min	30 min	60 min	240 min
Silverstein et al[10,b,c]	0.9% NaCl	80	10	60 (0.8)		28 (0.4)		14 (0.2)
	HSS	4	<1	13 (2.7)		9.6 (2.0)		2 (0.5)
	Dextran	20	3	18 (0.9)		28 (1.4)		20 (1.0)
	Hetastarch	20	3	21 (1.1)		28 (1.5)		20 (1.1)

[a]Not all studies evaluated plasma volume expansion at the same time intervals. Efficiency ratios were calculated as the ratio of the increase in blood volume (BV) to the volume of infused fluid as follows: (BV [mL] × percentage change in BV) ÷ volume of infused fluid (mL). The initial BV was assumed to be 80 mL/kg.
[b]These data were taken from the appendix of the cited study, where possible cardiovascular effects of HSS on normotensive, normovolemic dogs were evaluated.
[c]Data were presented as a percentage change in blood volume. The plasma volume expansion (mL/kg) was calculated by using an assumed 80-mL/kg blood volume and multiplying it by the percentage change in blood volume after each infusion.
HSS = hypertonic saline solution.

lower in cats treated with HSS. It has been proposed that HSS may lower MDF production and increase renal elimination of MDF by improving renal perfusion.[11]

HSS restored plasma volume, MAP, and CO to 80% of baseline in sheep with hemorrhagic shock, whereas 6% dextran 70 alone was not as effective.[7] The addition of a colloid to the HSS infusion resulted in a significantly higher CO during the 3-hour observation period. Similarly, dogs with experimental hemorrhagic shock showed significant improvements in cardiac index, arterial pressure, plasma volume, and PVR when resuscitated with either HSS or HSD; however, values tended to be more favorable after infusion of HSD.[8] These studies demonstrate that HSD increases and sustains CO and MAP more than HSS or dextran alone.

The lung vagal reflex has been proposed to be the mechanism of action responsible for the cardiac effects (e.g., increased CO) of HSS.[13] This reflex is important in circulatory control; however, it is unlikely to be entirely responsible for the effects of HSS on the cardiovascular system.[13] The improvements in cardiovascular function after HSS infusion are most likely due to the reestablishment of plasma volume expansion, but another variable, such as a reduction in MDF, may be involved.

Microvascular Effects

In hemorrhagic shock models, the reduction in circulating blood volume results in preferential vasoconstriction to reduce blood flow to nonvital organs.[14] In addition to vasoconstriction, one study demonstrated a further reduction in blood flow caused by endothelial cell swelling that progressively narrowed the capillary lumen.[14] The maintenance of cell volume is an active process requiring energy, and in conditions of shock, energy stores are depleted, leading to cell swelling. A vicious cycle of ischemia results from endothelial cell swelling, vasoconstriction, and further reductions in blood flow secondary to reduced blood volume. The administra-

tion of HSD during periods of ischemic shock significantly improved regional blood flow and reversed endothelial cell swelling, improving blood flow to vital organs, compared with administration of lactated Ringer solution.[14]

Shock also involves decreased splanchnic blood flow, which can be followed by intestinal ischemia. This decreased blood flow and ischemia can lead to mucosal damage and the release of microorganisms from the gut into systemic circulation (bacterial translocation). HSS have been shown to improve splanchnic blood flow, which may reverse ischemia and prevent bacterial translocation.[15]

Immunomodulatory Effects

Patients with hemorrhagic shock are at increased risk for bacterial translocation and sepsis from ischemic injury. One study attempted to identify the immune system's role in this process.[15] In hemorrhagic shock, neutrophils have been shown to have decreased phagocytic activity, while T lymphocytes and natural killer cells have reduced expression and activity. HSS infusions were shown to reverse suppression of lymphocytes and natural killer cells and to stimulate neutrophil phagocytic activity, which may further reduce bacterial translocation.[15]

Applications for Veterinary Patients

Much of the following information has been derived from an experimental setting with limited clinical evaluation. The use of HSS in these situations appears safe and efficacious, but additional clinical studies would be helpful to support HSS use as a standard of care.

Controlled Hemorrhagic Shock

The first applications of HSS therapy were in canine models of controlled hemorrhagic shock.[8] The infused volume, which was equal to only 10% of the blood lost (4 mL/kg), rapidly restored MAP and CO to baseline values. This effect

Key Facts

- Hypertonic saline solutions (HSS) are unique among crystalloids in their ability to provide immediate intravascular expansion, which can improve cardiac output, blood pressure, and perfusion to vital organs for patients in shock.

- HSS have been used for the initial resuscitation of patients with hemorrhagic shock, septic shock, and distributive shock, as well as those with head trauma, pulmonary contusions, and thermal injury.

- In addition to immediate plasma volume expansion, HSS have unique effects on the cardiovascular, microvascular, and immunologic systems.

- HSS are safe and effective for shock resuscitation at a dose of 2.5 to 5 mL/kg administered at a rate of ≤1 mL/kg/min.

- At the recommended dose, HSS appear to have no adverse effects on electrolyte concentration, osmolality, or coagulation.

was negligible at 180 minutes postinfusion. A similar model evaluating hemorrhagic shock in sheep showed similar improvements in MAP and CO, but the results were transient, lasting less than 30 minutes.[7] In the same model, a combination of a colloid and HSS resulted in sustained CO and MAP and lower PVR. In a study involving feline and murine models of hemorrhagic shock, HSS improved MAP, superior mesenteric artery blood flow, and CO for 15 to 75 minutes. When the HSS-resuscitated cats were reinfused with their hemorrhaged blood, these values were maintained at significantly higher levels compared with cats resuscitated with isotonic saline solution.[11]

Uncontrolled Hemorrhagic Shock

Studies have evaluated the use of HSS in uncontrolled hemorrhagic shock (UCHS).[16–18] Their results suggest that the use of HSS in UCHS increases bleeding, leads to a lower MAP, and leads to early mortality compared with isotonic crystalloid resuscitation. If UCHS can be converted into controlled hemorrhagic shock, then the use of HSS can raise MAP and improve survival.[16,17] The increase in bleeding seen with the use of HSS in UCHS is due to an initial spike in MAP, a decrease in systemic vascular resistance, and vasodilation. The increase in MAP and vascular wall tension forces the lacerated edges apart and leads to additional blood loss and an overall lower MAP.[16] It has also been shown that if a 4-mL/kg infusion of HSS is given over 12 minutes instead of 1 minute in UCHS, there is significantly less blood loss and increased survival.[18] However, HSS should be considered contraindicated in cases of UCHS due to the increased risk of bleeding and death.

Septic Shock

In a clinical study of septic shock secondary to pyometra in dogs,[19] the administration of HSD significantly increased MAP compared with resuscitation using isotonic saline solution. Both fluid types increased CO and cardiac index, but the volume of isotonic saline solution administered was eight times that of HSD. A decrease in glomerular filtration rate and urine production was noted in all patients; two of seven patients resuscitated with isotonic saline solution died of renal failure, whereas all seven patients resuscitated with HSD survived. Additional experimental studies of endotoxemic shock showed that HSS induced immediate and significant increases in CO, cardiac filling pressures, rates of oxygen delivery and consumption, stroke volume, and central venous pressure and decreases in pulmonary vascular resistance and that these effects could be sustained for up to 60 minutes.[20,21] Septic shock presents significant challenges for fluid resuscitation due to the effects of inflammatory mediators and cytokines on myocardial function, vascular tone, and endothelial permeability.[21] Colloids are frequently used to support intravascular volume in this setting, but HSS may have a role in the initial resuscitation of patients with septic shock.

Traumatic Brain Injury

Traumatic brain injury is a multifactorial disease involving a variety of pathophysiologic processes. It may be primary or secondary. Primary injury is related to the initial insult and may result in parenchymal hemorrhage, ischemia, compression, and/or direct neuronal injury. Primary injury cannot be altered and may trigger a number of processes that cause further (secondary) brain injury. Secondary brain injury involves changes caused by decreased cerebral blood flow and can be prevented or ameliorated by immediate resuscitation efforts to restore cerebral perfusion pressure (CPP) and prevent ischemic injury. The physiologic processes involved in secondary brain injury include cellular depletion of energy, disruption of cerebral blood flow, local inflammation in response to tissue damage, altered membrane function, reduced oxygen and nutrient delivery, and cerebral edema.[22] Restoring CPP is vital to the resuscitation of patients with head trauma. CPP is calculated using the following equation[23]:

$$CPP = MAP - ICP$$

Preserving CPP requires the maintenance of adequate MAP and the reduction of intracranial pressure (ICP). Patients with traumatic brain injury commonly present in shock; therefore, initial therapy must address cardiovascular status and hypotension. Aggressive crystalloid fluid therapy can elevate ICP by increasing fluid volume in the intracellular and interstitial compartments. This increase in ICP reduces the CPP and worsens secondary brain injury. HSS can restore MAP

and cardiovascular function as well as reduce ICP by pulling fluid from the extravascular space. Together, these effects may improve CPP and reduce secondary brain injury.[24]

In a study evaluating HSS resuscitation in sheep with hemorrhagic shock and induced brain injury, the overall fluid requirements and early ICP were lower for sheep resuscitated with HSS than for those resuscitated with lactated Ringer solution.[25] In a human study, patients with traumatic brain injury and hypotension who received HSD were twice as likely to survive as those who received lactated Ringer solution.[26]

Burns

Patients with thermal injury have unique fluid resuscitation needs, and treatment is complicated by increased vascular permeability resulting in large fluid shifts and edema within the first 24 hours.[27] Fluid therapy needs are the greatest during this period, and in human patients, delayed or inadequate resuscitation increases the risk of infection, organ failure, and mortality.[27,28] HSS are effective for the treatment of patients with burns because a small infusion volume can restore cardiovascular function and reduce total fluid requirements. Smaller fluid volumes are ideal in this setting to minimize edema and improve the chance of survival.[27]

Gastric Dilatation–Volvulus

Gastric dilatation–volvulus (GDV) is an acute, life-threatening condition that results in an obstructive, noncardiogenic shock associated with a mortality of approximately 16%.[29] As the stomach dilates, venous return decreases and blood is sequestered in the muscles, portal system, and splanchnic organs. CO and MAP subsequently decrease, so initial therapy should aim to expand intravascular volume and restore CO, MAP, and microvascular flow. In a recent retrospective study of 166 dogs with GDV,[29] hypotension was noted to be a risk factor significantly associated with death. The risk of hypotension could be significantly decreased if the patients were resuscitated with HSS or a synthetic colloid.[29] In 15 dogs with GDV-induced shock,[30] the administration of 5 mL/kg of HSD rapidly restored cardiovascular function to the same degree as 60 to 90 mL/kg of lactated Ringer solution. All dogs then received maintenance crystalloid fluid therapy at 20 mL/kg/h. The administration of HSD was not associated with any noticeable complications, and the authors concluded that it may be more efficient for cardiovascular resuscitation than crystalloids alone.[30]

Acute Pancreatitis

The use of HSS or HSD in resuscitating patients with acute pancreatitis may be superior to standard crystalloid therapy. Severe pancreatitis can compromise cardiovascular function and increase pulmonary endothelial permeability. The administration of large fluid volumes may result in pulmonary edema from disturbances within the pulmo-

Glossary of Common Fluid Therapy Terms[5,40]

- **Colloid:** A solution containing large molecules (>30,000 daltons) that do not readily cross the capillary membrane.

- **Colloid osmotic pressure (COP):** The osmotic pressure exerted at the capillary membrane by colloid molecules.

- **Extracellular fluid compartment:** Accounts for 33% of total body water; 25% is intravascular and 75% is interstitial.

- **Intracellular fluid compartment:** Accounts for 66% of total body water.

- **Osmolality:** The number of osmoles per kilogram of solvent (mOsm/kg).

- **Osmolarity:** The number of osmoles per liter of solution (mOsm/L). In clinical veterinary medicine, there is a negligible difference between osmolality and osmolarity.

nary bed, such as increased pulmonary vascular resistance, pulmonary hypertension, and decreased pulmonary blood flow. In a canine model of acute, bile-induced pancreatitis, resuscitation with HSD effectively restored cardiac function and reduced pulmonary edema with lower total fluid requirements.[31]

Several murine studies have examined the local and systemic effects of experimentally induced acute pancreatitis. Animals resuscitated with HSS showed a reduction in pancreatic necrosis and infection, attenuation of end-organ injury following a systemic inflammatory response, and improved survival.[32,33] However, the use of HSS in acute pancreatitis is a novel application, and evidence regarding its efficacy and safety is insufficient to recommend it at this time.

Complications and Contraindications
Electrolytes and Osmolality

The effects of HSS infusions on electrolytes and osmolality were evaluated in a canine study.[34] The administration of 2.5 mL/kg or 5 mL/kg of HSS produced transient elevations in sodium (<160 mmol/L; normal, 140 mEq/L), chloride (<130 mmol/L; normal, 110 mEq/L), and osmolality (>320 mOsm/kg H_2O; normal range, 290 to 310 mOsm/kg) for 5 minutes postinfusion. Administration of a 15-mL/kg bolus produced hypernatremia (>160 mmol/L), hyperchloremia (>130 mmol/L), and hyperosmolality (>340 mOsm/kg H_2O) for up to 90 minutes postinfusion. HSS can also produce transient hypokalemia (>4 mEq/L) with doses from 2.5 to 15 mL/kg.[34] Potassium regulation is complex, but aggressive fluid therapy with any potassium-free solution can result in hypokalemia from the translocation of potassium from the extracellular to the intracellular fluid compartment and increased urinary

BOX 1

Initial Fluid Selection and Dosing for Trauma Patients With Hemorrhagic Shock[43,a]

1. Administer initial resuscitation fluids:

- **Mild hemorrhage** (<20% blood loss, pale mucous membranes, CRT <2 sec, strong pulses, normal MAP): Isotonic crystalloid (dog, 20–30 mL/kg; cat, 10–20 mL/kg)

- **Moderate hemorrhage** (20%–40% blood loss, pale mucous membranes, fair pulses, tachycardia): Isotonic crystalloid (dog, 20–30 mL/kg; cat, 10–20 mL/kg) *or* colloid (5–10 mL/kg)

- **Severe hemorrhage** (>40% blood loss, white mucous membranes, CRT >2 sec, tachycardia, decreased MAP, hypothermic): HSS/HSD (2–4 mL/kg bolus[a]) *and* isotonic crystalloid (dog, 20–30 mL/kg; cat, 10–20 mL/kg)

- **Catastrophic hemorrhage** (>50% blood loss, CRT >3 sec, poor or absent peripheral pulses, decreased MAP, tachycardia or bradycardia): HSS/HSD (4 mL/kg bolus) *and* isotonic crystalloid (dog, 40–90 mL/kg; cat, 30–60 mL/kg)

- **Shock with head trauma**, neurologic dysfunction and/or cranial nerve deficits: HSS/HSD or colloid (2–4 mL/kg) *or* isotonic crystalloid (dog, 35–55 mL/kg; cat, 24–36 mL/kg)

2. Assess patient for the following cardiovascular end points:

- Pink mucous membranes
- CRT <2 sec
- Normal heart rate
- Normal MAP
- Improved pulse quality
- Normal body temperature
- COP >14 mm Hg
- CVP 6–8 cm H_2O
- Urine output >1 mL/kg/h
- Improved neurologic status
- Improved oxygenation

3. If the above end points are not met, continue resuscitation efforts:

- In patients without head trauma:
  —If PCV >15%, consider HSS/HSD (2–4 mL/kg) or hetastarch (5–10 mL/kg)
  —If PCV <15%, consider pRBCs (5–10 mL/kg) or HBOC (5–10 mL/kg)

- In patients with head trauma, consider mannitol (1–2 g/kg)

- Reassess cardiovascular end points

4. If the above end points are met, continue with maintenance fluids. Reassess end points frequently.

CRT = capillary refill time; *COP* = colloid osmotic pressure, *CVP* = central venous pressure; *HBOC* = hemoglobin-based oxygen carrier; *HSD* = hypertonic saline with dextran; *HSS* = hypertonic saline solution; *MAP* = mean arterial pressure; *PCV* = packed cell volume; *pRBCs* = packed red blood cells.
[a]Fluid therapy recommendations are for dogs and cats unless otherwise stated.

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potassium excretion.[35] Electrolytes and osmolality should be monitored when using HSS or aggressive fluid therapy due to the major shifts in sodium and water across fluid compartments. If osmolality cannot be measured directly, it can be approximated as twice the sodium concentration.[3] The use of HSS is contraindicated in patients with significant hypernatremia, hyperosmolality, hyperchloremia, or hypokalemia.[3]

Dehydration

Dehydration has been considered a contraindication to the use of HSS. Several studies have evaluated the effect of HSS resuscitation in patients with dehydrated hemorrhagic shock. All studies showed that HSS were as effective as crystalloids in restoring MAP, CO, blood flow, and plasma volume in these patients with no adverse effects.[36,37] However, although dehydration may not be an absolute contraindication to HSS administration, HSS are more commonly used for acute-onset shock states. If HSS were administered in the setting of dehydration for immediate intravascular volume expansion, it would be necessary to then administer isotonic fluids to replenish the interstitial and intracellular fluid compartments.

Coagulation and Fibrinolysis

The effect of HSS on the coagulation and fibrinolytic cascade of human plasma in vitro has been analyzed with thromboelastography.[38,39] Prothrombin time, activated prothrombin time, and platelet aggregation were significantly elevated when >10% of the plasma volume was replaced with HSS. The results of this study suggested that clot formation was delayed, but the clot quality was unaffected.[38] A dog's plasma volume is approximately 5% of its body weight, or 48 mL/kg. Plasma volumes in cats are estimated to be 37 to 49 mL/kg.[40] Infusions exceeding 5 mL/kg replace >10% of the plasma volume and may prolong clotting.

The authors of a study that used human whole blood[39] to evaluate coagulation and fibrinolysis in vitro by replacing 5% of the blood volume with HSS noted no significant differences in any thromboelastographic parameters. They concluded that HSS have anticoagulant effects if they replace >7.5% of the whole blood sample. A cat's blood volume is 6% to 7% of its body weight (62 to 66 mL/kg); a dog's is 8% to 10% of its body weight, or 77 mL/kg.[40] Infusions of HSS exceeding 5.7 mL/kg replace >7.5% of the blood volume and may result in clinical coagulopathies.

These studies were performed in vitro and may not accu-

rately represent the clinical effects of HSS. HSS should be used with caution in patients with clinical coagulopathies, thrombocytopenia, or platelet dysfunction due to their potential to prolong clotting times and delay clot formation, especially if the recommended dosage is exceeded.

Recommended Dosage and Rate of Infusion

When administered as a single infusion at the recommended dosage of 2.5 to 5 mL/kg and a rate ≤1 mL/kg/min, HSS (7%) appear to be safe and effective for fluid therapy. Higher rates may be associated with a substantial decrease in MAP from arteriolar vasodilation and with a reduction in PVR and vagally mediated bradycardia for <1 minute.[1,41] These effects are usually transient and resolve with slowing of the infusion rate, but they can be problematic in a patient that is already in critical condition.[42] Infusions of a hyperosmolar solution (up to 7%) into a peripheral vein have been deemed safe, but hemolysis can occur with 10% to 23% HSS infusions.[42] HSS do not appear to injure tissues when administered perivascularly.[13] HSS should not be administered as constant-rate infusions until further evaluated. **BOX 1** suggests an initial fluid therapy protocol for immediate resuscitation of patients with hemorrhagic shock or head trauma.

Commercially formulated HSD should be administered at a dose of 2 to 6 mL/kg. If necessary, HSD can be created by diluting 23.4% HSS with a colloid at a ratio of 1:2.5.[43] Alternatively, the components of HSD can be combined into a single syringe or administered separately using the following formula:

2–6 mL/kg of 7% NaCl +
4–6 mL/kg of 6% dextran 70 or hetastarch

The initial dose of each component should be selected based on cardiovascular parameters representing the severity of the shock.

Conclusion

HSS are likely to be beneficial in the initial resuscitation of patients with controlled hemorrhagic, septic, and distributive shock, as well as patients with head trauma and burn injury. Additional studies of the use of HSS in the treatment of acute pancreatitis are needed.

HSS are unique among crystalloid solutions in their ability to provide rapid intravascular volume expansion and improved cardiovascular, microvascular, and immune function. They may improve perfusion and reduce the risk of bacterial translocation. HSS (7%) appear to be well tolerated without complications at the recommended dose of 2.5 to 5 mL/kg administered at a rate of ≤1 mL/kg/min, and their effects persist for 1 to 3 hours. The addition of a colloid (e.g., dextran, hetastarch) can prolong the effects beyond 3 hours.

HSS are used mainly for immediate resuscitation of

intravascular volume. Because their effects are transient, it is always appropriate to subsequently administer colloids, crystalloids, or both. The type of fluid and the volume required vary by patient. Resuscitation of patients in shock is directed at restoring physical parameters such as heart rate, mucous membrane color, capillary refill time, pulse quality, mental alertness, and urine output to normal levels. Measured parameters, including blood pressure and central venous pressure, are helpful in determining whether fluid resuscitation is adequate. The cardiovascular effects after the initial bolus of HSS are transient, and because patients may decompensate after initial stabilization, careful monitoring should continue even if resuscitation end points have been reached. With early recognition and aggressive fluid resuscitation, practitioners can improve outcomes for patients in shock by incorporating HSS, when appropriate, into their resuscitation protocols.

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1. Which statement is true with regard to HSS?
a. Their osmolarity exceeds that of plasma.
b. They contain insignificant concentrations of potassium and magnesium.
c. They contribute to colloid osmotic pressure.
d. They contain a buffer.

2. HSS infusions are used primarily for their effect on the _____ compartment.
a. interstitial
b. intravascular
c. intracellular
d. all of the above

3. The cardiovascular effect(s) of HSS infusions is/are
a. increased MAP.
b. reduced PVR.
c. increased CO.
d. all of the above

4. How do HSS primarily improve cerebral perfusion pressure?
a. They increase intracranial pressure.
b. They increase MAP.

c. They reduce local inflammation.
d. They alter cell membrane function.

5. The recommended rate of administration for HSS is _____ mL/kg/min.
a. ≤1
b. 2.5 to 5
c. 10
d. 20

6. HSS, given at the recommended dose, are associated with
a. transient elevations in sodium levels.
b. transient hyperosmolality.
c. hemolysis.
d. a and b

7. The use of HSS is contraindicated in patients with significant
a. hyperchloremia.
b. hypernatremia.
c. hyperosmolarity.
d. all of the above

8. HSS infusions can result in plasma volume expansion for up to
a. 30 minutes.
b. 1 hour.

c. 90 minutes.
d. 3 hours.

9. Which statement(s) is/are true regarding the use of HSS in controlled hemorrhagic shock?
a. They increase MAP.
b. They increase superior mesenteric artery blood flow.
c. They increase CO.
d. all of the above

10. Which statement is true regarding the effects of HSS?
a. Plasma volume expansion is related to the movement of intracellular fluid directly into the intravascular space.
b. HSS infusions improve regional blood flow by reversing endothelial cell swelling.
c. HSS reduce the risk of bacterial translocation by decreasing phagocytic activity of lymphocytes and natural killer cells.
d. HSS can improve MAP in uncontrolled hemorrhagic shock.