PEDIATRIC AND INFANT SHOCK

The Task Force reviewed evidence related to several key questions about the management of shock in children. There is ongoing uncertainty about the indications for using colloid versus crystalloid in shock resuscitation. One large adult trial suggested that normal saline (isotonic crystalloid) is equivalent to albumin, although subgroup analysis suggested harm associated with the use of colloid in patients with traumatic brain injury. There were insufficient data to change the 2005 recommendations.

The optimal timing for intubation of children in shock remains unclear, although reports of children and adults with septic shock suggested potential beneficial effects of early intubation (before signs of respiratory failure develop) combined with a protocol-driven management approach. When children in septic shock were treated with a protocol that included therapy directed to normalizing central venous oxygen saturation, patient outcome appeared to improve.

Performing rapid sequence induction and tracheal intubation of a child with shock can cause acute cardiovascular collapse. Etomidate typically causes less hemodynamic compromise than other induction drugs and is therefore often used in this setting. However, data suggest that the use of this drug in children and adults with septic shock is associated with increased mortality that may be secondary to etomidate's inhibitory effects on corticosteroid synthesis. Administering stress-dose corticosteroids in septic shock remains controversial, with recent adult trials failing to show a beneficial effect.

Graded Volume Resuscitation for Hemorrhagic Shock[Peds-032]

Consensus on Science

There are no pediatric studies of the timing or extent of volume resuscitation in hemorrhagic shock with hypotension. Nine LOE 5 adult[387,-,395] studies reported conflicting results with regard to the effect of timing and extent of volume resuscitation on outcome of hemorrhagic shock with hypotension.

Treatment Recommendations

There is insufficient evidence as to the best timing or quantity for volume resuscitation in infants and children with hemorrhagic shock following trauma.

Knowledge Gaps

What is the appropriate clinical indicator for volume resuscitation during treatment of hemorrhagic shock in infants and children?

Early Ventilation in Shock[Peds-038B]

Consensus on Science

There are no studies investigating the role of intubation and assisted ventilation before the onset of respiratory failure in infants and children with shock. Two LOE 5 animal studies in septic shock[396,397] and 1 LOE 5 animal study in pericardial tamponade[398] showed improved hemodynamics and select organ perfusion with intubation before the onset of respiratory failure. One report of 2 adult patients[399] (LOE 5) described cardiac arrest following intubation of 1 adult patient with tamponade

due to penetrating trauma and improvement in hemodynamics during spontaneous breathing in 1 mechanically ventilated adult patient with post-cardiac surgery tamponade.

One LOE 5 study of septic shock in adults[400] suggested a reduced mortality with early ventilation compared with historic controls who only received ventilation for respiratory failure. One LOE 5 study of animals in septic shock[401] showed that early assisted ventilation does not reduce oxygen extraction or prevent the development of lactic acidosis.

Treatment Recommendations

There is insufficient evidence to support or refute the use of endotracheal intubation of infants and children in shock before the onset of respiratory failure.

Knowledge Gaps

Does the timing of respiratory support in infants and children with shock affect outcome?

Colloid Versus Crystalloid Fluid Administration[Peds-044A,Peds-044B]

Consensus on Science

Evidence from 3 randomized blinded LOE 1 controlled trials in children with dengue shock syndrome[402,-,404] and 1 LOE 1 open randomized trial in children with septic shock[405] suggested no clinically important differences in survival from therapy with colloid versus therapy with isotonic crystalloid solutions for shock.

In 1 large LOE 5 randomized controlled trial of fluid therapy in adult ICU patients[406] and in 6 good-quality LOE 5 meta-analyses, predominantly of adults,[407,-,412] no mortality differences were noted when colloid was compared with hypertonic and isotonic crystalloid solutions, and no differences were noted between types of colloid solutions.

Three LOE 5 studies comparing the use of crystalloids and colloids for adults in shock suggested that crystalloid may have an associated survival benefit over colloid in subgroups of patients with shock, including general trauma,[409] traumatic brain injury,[413] and burns.[414] One randomized controlled LOE 5 study of children with severe malaria suggested better survival with colloid than with crystalloid infusion.[415]

Treatment Recommendations

Isotonic crystalloids are recommended as the *initial* resuscitation fluid for infants and children with any type of shock. There is insufficient evidence to identify the superiority of any specific isotonic crystalloid over others.

Knowledge Gaps

Does the use of any specific crystalloid solution (Ringer's lactate, normal saline, hypertonic saline) improve outcome for pediatric shock? Are there subgroups of children in shock whose outcome is improved with the use of colloid compared with crystalloid?

Vasoactive Agents in Distributive Shock[Peds-045A,Peds-045B]

Consensus on Science

One LOE 4 observational study[416] suggested that the course of pediatric septic shock physiology is dynamic and that serial assessments are required to titrate the type and dose of inotropes or vasopressor therapy to achieve optimal hemodynamic results. Evidence from 4 LOE 1 pediatric randomized controlled studies,[417,-,420] 3 LOE 5 adult randomized controlled studies,[421,-,423] and 1 LOE 5 adult systematic review[424] showed that no inotrope or vasopressor is superior in reducing mortality from pediatric or adult distributive shock.

Two LOE 1 pediatric randomized controlled studies[417,418] showed that children with "cold" (ie, low cardiac index) septic shock improved hemodynamically with brief (4-hour) administration of milrinone (bolus and infusion). One LOE 1 pediatric randomized controlled study[420] of vasodilatory shock compared the addition of vasopressin versus placebo to standard vasoactive agents and showed no change in duration of vasopressor infusion but observed a trend toward increased mortality.

Eleven small LOE 4 pediatric case series[425,-,435] showed improved hemodynamics but not survival when vasopressin or terlipressin was administered to children with refractory, vasodilatory, septic shock.

Treatment Recommendations

There is insufficient evidence to recommend a specific inotrope or vasopressor to improve mortality in pediatric distributive shock. Selection of an inotrope or vasopressor to improve hemodynamics should be tailored to each patient's physiology and adjusted as clinical status changes.

Knowledge Gaps

Does the use of any specific vasoactive agent improve outcome for infants and children with distributive shock?

Vasoactive Agents in Cardiogenic Shock[Peds-046A]

Consensus on Science

One LOE 4 pediatric case series[436] showed that critically ill children requiring inotropic support have wide variability in hemodynamic responses to different infusion rates of dobutamine. One LOE 2 blinded crossover study[437] found dopamine and dobutamine had equal hemodynamic effects in infants and children requiring post-cardiac surgical inotropic support but that dopamine at an infusion rate of >7 mcg/kg per minute increased pulmonary vascular resistance.

Six LOE 3 studies[438,-,443] showed that both dopamine and dobutamine infusions improve hemodynamics in children with cardiogenic shock.

Evidence from 1 LOE 1 pediatric placebo-controlled trial[444] showed that milrinone is effective in preventing low cardiac output syndrome in infants and children following biventricular cardiac repair. One LOE 4 study[445] showed that milrinone improved cardiac index in neonates with low cardiac output following cardiac surgery.

One small LOE 1 study[446] showed that children had better hemodynamic parameters and shorter ICU stays if they received milrinone compared with low-dose epinephrine plus nitroglycerin for inotropic support following repair of tetralogy of Fallot.

In 2 LOE 4 small case series,[447,448] when children with heart failure secondary to myocardial dysfunction were given levosimendan, they demonstrated improved ejection fraction, required a shorter duration of catecholamine infusions,[447] and showed a trend toward improved hemodynamics and reduced arterial lactate levels.[448]

In subgroup analysis from 1 LOE 5 randomized controlled trial in adults,[449] patients with cardiogenic shock treated with norepinephrine versus dopamine had an improved survival at 28 days. When all causes of shock were included, patients treated with norepinephrine also had fewer arrhythmias than those treated with dopamine (12% versus 24%).

Treatment Recommendations

The catecholamine dose for inotropic support in cardiogenic shock must be individually titrated because there is a wide variability in clinical response. It is reasonable to use epinephrine, levosimendan, dopamine, or dobutamine for inotropic support in infants and children with cardiogenic shock. Milrinone may be beneficial for the prevention and treatment of low cardiac output following cardiac surgery.

There are insufficient data to support or refute the use of norepinephrine in pediatric cardiogenic shock.

Knowledge Gaps

Does the use of any specific vasoactive agent improve outcome for infants and children with cardiogenic shock who have not undergone cardiac surgery?

Etomidate for Intubation in Hypotensive Septic Shock[Peds-047A,Peds-047B]

Consensus on Science

One LOE 4 study of children with septic shock[450] showed that adrenal suppression occurred after the administration of a single dose of etomidate and persisted for at least 24 hours. Evidence from 2 LOE 4[451,452] studies and 1 LOE 5[453] study showed that etomidate can be used to facilitate tracheal intubation in infants and children with minimal hemodynamic effect, but very few of these reports included patients with hypotensive septic shock. One LOE 4 study[450] suggested an association with mortality when etomidate is used to facilitate the intubation of children with septic shock.

One adult LOE 5 study[454] observed an increased mortality associated with the use of etomidate for intubation of patients in septic shock, even with steroid supplementation. Conversely, 1 underpowered adult LOE 5 study[455] in septic patients did not show an increase in mortality.

One multicenter adult LOE 5 comparative trial of etomidate versus ketamine for intubation[456] found no difference in organ failure over the first 72 hours and no mortality difference, but this study included only a small number of patients with shock. Adrenal insufficiency was more common in etomidate-treated patients.

Treatment Recommendations

Etomidate should not be routinely used when intubating an infant or child with septic shock. If etomidate is used in infants and children with septic shock, the increased risk of adrenal insufficiency should be recognized.

Knowledge Gaps

If etomidate is used, does steroid administration improve outcome for infants and children with septic shock?

Corticosteroids in Hypotensive Shock[Peds-049A,Peds-049B]

Consensus on Science

In 6 LOE 5 randomized controlled trials in adults with septic shock[454,457,-,461] the addition of low-dose hydrocortisone decreased the time to shock reversal. Three LOE 5 randomized controlled trials in adults with vasopressor-dependent septic shock[457,462,463] showed that survival was improved when low-dose hydrocortisone was administered, while 1 small adult LOE 5 randomized controlled trial[464] showed a trend toward increased survival.

One fair-quality, small LOE 1 study in children with septic shock[465] found that low-dose hydrocortisone administration resulted in no survival benefit. One fair-quality LOE 1 study of administration of low-dose hydrocortisone to children with septic shock[466] demonstrated earlier shock reversal. Data from 1 LOE 4 hospital discharge database[467] noted the association between the use of steroids in children with severe sepsis and decreased survival.

In 1 LOE 5 study in adults with septic shock[457] survival improved significantly with the use of low-dose hydrocortisone and fludrocortisone compared with placebo. Conversely 4 LOE 5 adult trials in septic shock[454,459,-,461] showed no survival benefit with low-dose corticosteroid therapy. In 1 large LOE 5 randomized controlled trial of adults in septic shock,[454] corticosteroid administration was associated with an increased risk of secondary infection.

Treatment Recommendations

There is insufficient evidence to support or refute the routine use of stress-dose or low-dose hydrocortisone and/or other corticosteroids in infants and children with septic shock. Stress-dose corticosteroids may be considered in children with septic shock unresponsive to fluids and requiring vasoactive support.

Knowledge Gaps

What is the appropriate “stress dose” of hydrocortisone for hypotensive septic shock? Should the dose of hydrocortisone be titrated to the degree of shock? Should an adrenocorticotrophin (ACTH) stimulation test be performed to determine if an infant or child in septic shock has adrenal insufficiency?

Diagnostic Tests as Guide to Management of Shock[Peds-050A,Peds-050B]

Consensus on Science

In 1 LOE 1 randomized controlled trial in children with severe sepsis or fluid-refractory septic shock,[468] protocol-driven therapy that included targeting a superior vena caval oxygen saturation >70%, coupled with treating clinical signs of shock (prolonged capillary refill, reduced urine output, and reduced blood pressure), improved patient survival to hospital discharge in comparison to treatment guided by assessment of clinical signs alone.

Two LOE 5 studies of adults with septic shock, one a randomized controlled trial[469] and the other a cohort study,[470] documented improved survival to hospital discharge following implementation of protocol-driven early goal-directed therapy, including titration to a central venous oxygen saturation ($ScvO_2$) ≥70%. In 1 large multicenter LOE 5 adult study[471] evaluating the "Surviving Sepsis" bundle, early goal-directed therapy to achieve an $ScvO_2$ ≥70% was not associated with an improvement in survival, but venous oxygen saturations were measured in <25% of participants.

There are insufficient data on the utility of other diagnostic tests (eg, pH, lactate) to help guide the management of infants and children with shock.

Treatment Recommendations

A protocol-driven therapy, which includes titration to a superior vena caval oxygen saturation ≥70%, may be beneficial for infants and children (without cyanotic congenital heart disease) with fluid-refractory septic shock. No treatment recommendations can be made to target $ScvO_2$ saturation in the management of fluid-refractory septic shock in pediatric patients with cyanotic congenital heart disease or for other forms of pediatric shock.