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Helping children survive sepsis

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IN 2005, MORE THAN 75,000 children were hospitalized for severe sepsis at a cost of $4.8 billion, and the incidence continues to increase.[1] The monetary expense is staggering, but the morbidity and mortality associated with severe sepsis in children is even more alarming.

Farris et al. studied 28-day functional outcomes for pediatric patients with severe sepsis who required mechanical ventilation and at least one inotropic or vasopressor infusion. The results showed that 46% of the 466 subjects had a decline in functional status, and that 32% didn't survive or had a poor functional outcome at 28 days.[2] In light of these alarming statistics, much of the literature highlights the importance of continued research. Also, the results of adult studies many times don't translate into the same results in the pediatric population.[2-4] Knowledge that children are not just little adults should guide interventions and treatment for pediatric sepsis. (See *Understanding sepsis*.)

This article highlights the most current sepsis definitions and incorporates pediatric considerations as outlined in the most recent guidelines from the Surviving Sepsis Campaign (SSC), including evidence-based nursing considerations. The pediatric guidelines are targeted toward term newborns and children; guidelines for preterm infants are beyond the scope of this article.

Promoting education and best practices

The SSC is a movement by the international healthcare community to review and disseminate information on best practices in the treatment of severe sepsis and septic shock. The SSC's goal is providing education to reduce sepsis-associated mortality and ultimately to decrease the incidence and burden that sepsis causes.[5]

The SSC guidelines were first published in 2004 and have been updated twice, most recently in 2012. They're not limited to medical interventions; nursing plays an integral role in policy and procedure development and revision, and may also influence product choice and selection, such as colloid versus crystalloid administration.[6]

The authors of the SSC guidelines clearly denote the difference between managing pediatric and adult patients. While the breadth of the guidelines could be applied to septic patients across the lifespan, the literature

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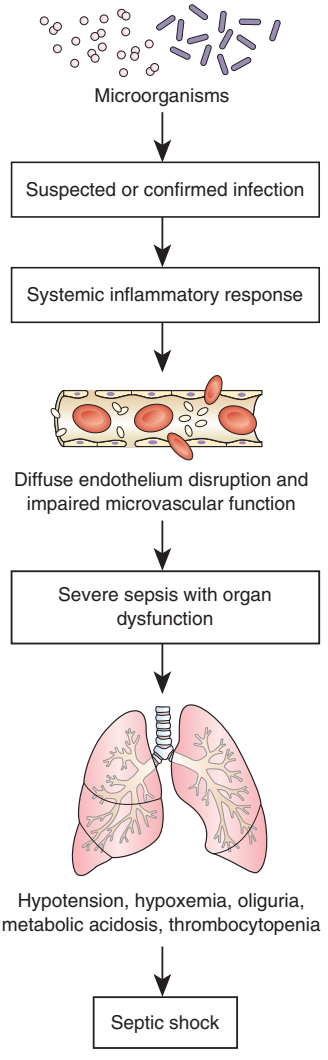
Understanding sepsis[6]

Infection causes changes that threaten to interfere with the function of each body system and triggers a cascade of events that even modern medication can't always prevent or stop. Microorganisms that enter the body release toxins that damage host tissues, releasing host chemical mediators that, in an attempt to stop further damage, can actually cause tissue damage. The end results of this cascade of events include abnormal blood volume distribution, cardiac dysfunction, imbalance between oxygen supply and demand, and metabolic disturbances.



points out that interventions recommended for adults aren't always appropriate for children.[5] According to the guidelines, pediatric definitions of sepsis, severe sepsis, septic shock, and multiple organ dysfunction/failure syndromes are similar to adult definitions but depend upon age-specific heart rate, respiratory rate, and white blood cell (WBC) count values.

In 2002, the International Pediatric Sepsis Consensus Conference modified the definitions for pediatric systemic inflammatory response syndrome (SIRS), infection, severe sepsis, and septic shock. These are considered the standard definitions for pediatrics and were referenced in the SSC guidelines. (See *Defining sepsis in children*.)[7]

Initial resuscitation

The algorithm for stepwise management of hemodynamic support in infants and children provides an overview of the best practices for treatment of pediatric sepsis according to time. Referenced by the SSC guidelines, this algorithm was initially developed by the American College of Critical Care Medicine and published in the journal *Critical Care Medicine* in 2009.[8] The timeframe provides an important context for the need for rapid intervention as soon as sepsis is suspected or identified. Interventions must begin immediately, in the ED if necessary.[8]

The initiation of early goal-directed therapy is consistently discussed in the literature as a critical factor in positive outcomes for children with sepsis.[4,9] Goals or endpoints for treatment are directed toward maintaining oxygenation and ventilation and achieving normal perfusion.

In the absence of advanced hemodynamic monitoring, initial therapeutic goals of septic shock resuscitation include:

- capillary refill of 2 seconds or less
- normal pulses with equal central and peripheral pulses
- warm extremities
- normal mental status
- urine output greater than 1 mL/kg/hour
- normal BP for age
- normal serum glucose and ionized calcium levels.[4]

In the presence of advanced hemodynamic monitoring, initial therapeutic goals include central venous oxygen saturation greater than or equal to 70%, and cardiac index between 3.3 and 6.0 L/min/meter^2.[4]

Ranjit et al. examined the use of invasive BP monitoring in combination with bedside echocardiography to better determine fluid status and myocardial dysfunction. They found that our traditional endpoints may not be entirely accurate predictors and that further investigation is needed.[10]

Children in septic shock may or may not present with elevated lactate levels, so therapeutic endpoints for pediatric sepsis don't include lactate clearance. Also, it's important to remember that children may be able to compensate for hypotension with an increased heart rate, and that normotension doesn't signal an absence of sepsis or indicate that resuscitation is successful.[5] Clinical nurses should constantly assess the patient for either achievement or deterioration in multiple endpoints not limited to BP.

Initial respiratory interventions for a child with sepsis include administration of supplemental oxygen via face mask or high-flow nasal cannula. The child may progress quickly into further respiratory distress and require nasopharyngeal continuous positive airway pressure as a bridge to provide adequate oxygenation and ventilation while the child is receiving initial fluid resuscitation.[5]

Fluid resuscitation begins with isotonic crystalloid solution or albumin administration in increments of up to 20 mL/kg boluses over 5 to 10 minutes. Large fluid deficits may require 40 to 60 mL/kg or more in the absence of signs of fluid overload.[5]

The merits of colloid solutions versus crystalloid haven't been proven in research. The availability and lower cost of crystalloid solutions make them a more favorable choice for initial resuscitation in a child without known cardiovascular disease.[4]

In pediatric patients, initial fluid administration can be complicated by the difficulty of establishing peripheral venous access, especially in patients experiencing fluid volume deficit and peripheral vasoconstriction. While central venous access is the ultimate goal, the time and sedation needed to obtain this may impede rapid initiation of treatment. To prevent delays, intraosseous access is often a first choice until more stable central venous access is an option.[5]

Another important consideration is administration of fluid boluses as quickly as possible, ideally over 5 to 10 minutes, by hand via syringe or via rapid infuser rather than an I.V. pump, which may not be able to provide an adequate administration rate.[9]

Fluid resuscitation may lead to or exacerbate respiratory distress as a result of fluid volume overload. But adequate fluid resuscitation is necessary to prevent cardiovascular complications secondary to increased intrathoracic pressure and reduced venous return during mechanical ventilation. Thus, prioritization and reprioritization must occur to ensure that a patient's oxygen demands are being met during fluid resuscitation. Infants and small children may require early endotracheal intubation due to a low functional residual capacity and inability to tolerate fluid volumes necessary for resuscitation.[5]

A child's fluid status can be assessed by the endpoints of treatment as discussed above. Signs of fluid overload in children include hepatomegaly and pulmonary crackles. Per the guidelines, if fluid overload occurs, fluid boluses should be discontinued and inotropic support initiated.[5]

Antibiotic administration

Best practices concerning antibiotic administration include timeliness, drug choice, and route of administration. Inappropriate antibiotics, failure to control the source of infection, and retained infected devices are associated with increased mortality in children.[5]

Although blood culture specimens should ideally be obtained before antibiotic administration, empiric antibiotic therapy should be administered within the first hour that severe sepsis is identified regardless of whether or not culture specimens have been obtained. Increased mortality is associated with delays in antibiotic administration. Antibiotics may be administered I.M. or orally (if appropriate) if I.V. access is delayed or isn't feasible in the early resuscitation period.[5]

Antibiotic selection should be based on the potential source of

Defining sepsis in children[7]

Systemic inflammatory response syndrome (SIRS)

The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count:

- Core temperature of greater than 38.5° C (101.3° F) or less than 36° C (96.8° F).
- Tachycardia, defined as a mean heart rate greater than 2 SD above normal for age in the absence of external stimuli, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5- to 4-hr time period or for children less than 1 yr old; bradycardia, defined as a mean heart rate less than 10th percentile for age in the absence of external vagal stimuli, beta-blockers, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5-hr time period.
- Mean respiratory rate greater than 2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anesthesia.
- Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or greater than 10% immature neutrophils.

Infection

A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen or a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or lab tests (for example, WBCs in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash, or purpura fulminans).

Sepsis

SIRS in the presence of or as a result of suspected or proven infection.

Severe sepsis

Sepsis plus one of the following: cardiovascular organ dysfunction or acute respiratory distress syndrome or two or more other organ dysfunctions.

Septic shock

Sepsis and cardiovascular organ dysfunction.

infection, if known. The nurse plays a crucial role in thoroughly assessing the child presenting in sepsis for potential sources of infection, such as abscess, necrotizing fasciitis, empyema, or necrotizing pneumonia.[5]

Inotropes and vasoactive drugs

Prior to studies in the early 2000s, starting inotrope or vasopressor infusions before obtaining central venous access in children wasn't recommended due to the potential for infiltration and local tissue injury.[8] Although central venous access can be difficult to obtain in children, the risks associated with peripherally administered inotrope or vasopressor therapy don't outweigh the benefit of early vasopressor administration. Vasopressors should be administered peripherally until central venous access can be obtained. Children with sepsis may present in various hemodynamic states, and in fact may vacillate between high and low cardiac output and high and low systemic vascular resistance.[5]

The choice of therapeutic agent or combination of agents depends on the child's hemodynamics and the recommendations in the American College of Critical Care Medicine-Pediatric Advanced Life Support guidelines for management of septic shock.[8] Of note, there is debate in the literature regarding each of the traditional vasoactive drugs of choice. Dopamine has recently been shown to suppress neutrophilic activity and interfere with neuroendocrine activity, both of which may actually increase susceptibility to infection.[4] Although all therapeutic interventions have risks and benefits, traditional inotropic agents such as dopamine may not be the best choice for the patient in septic shock.[4] The SSC guidelines do recommend administering a vasodilator (such as milrinone, amrinone, or enoximone) in addition to

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inotropes for select patients with persistent low cardiac output states associated with high systemic vascular resistance and normal BP.[5]

Once vascular access is established, fluid resuscitation is initiated, antibiotics are administered, and respiratory support is in place, the patient should be transferred to an ICU if he or she hasn't reached one of the above endpoints of treatment. If an endpoint is reached, the patient must still be closely monitored for resolution of signs and symptoms.[9]

In the ICU, fluid resuscitation will continue as the patients' clinical status dictates. Vasoactive infusions may continue as indicated, an antibiotic regimen should be determined, and electrolyte abnormalities should be corrected.

Secondary treatment and supportive care in the ICU include corticosteroids, blood products/plasma therapies, sedation, analgesia, mechanical ventilation, glycemic control, diuretics and renal replacement therapy (RRT), nutrition, and psychosocial support.[5] Extracorporeal membrane oxygenation should be considered for a child with refractory respiratory failure associated with sepsis or refractory septic shock.[5,11]

Corticosteroids

Hydrocortisone therapy is indicated in patients with adrenal insufficiency who present with fluid-refractory, catecholamine-resistant shock, but it isn't indicated for routine use. About 25% of children presenting in septic shock will have adrenal insufficiency. Risk factors for adrenal insufficiency include previous steroid therapy, septic shock with purpura, and known adrenal or pituitary abnormalities.[5] The REsearching severe Sepsis and Organ Dysfunction in children: a gLobal perspective (RESOLVE) study found no significant difference in outcomes in pediatric patients in severe septic shock whether or not they received hydrocortisone therapy. Although this wasn't the RESOLVE study's primary purpose, it's the largest pediatric sepsis clinical trial documented and included 477 patients.[12]

Blood products/ plasma therapies

Initial hemoglobin targets during the acute period of shock with hypoxemia should be 10 g/dL, which is similar to the recommendation for adults. After stabilization, a lower threshold (7 g/dL) is permissible. The nurse should always be mindful of the risks associated with transfusion and aware of the recommended hemoglobin targets.[5,13]

Plasma administration is recommended for patients with coagulopathy after the initial resuscitation period, keeping in mind that appropriate fluid resuscitation should

ideally reverse disseminated intravascular coagulation.[5] Conclusive evidence indicates that coagulopathy is associated with increased mortality in the septic patient; continued research in this area is needed.[3]

Mechanical ventilation

Many children with fluid-refractory sepsis require invasive mechanical ventilation for reasons discussed earlier, such as fluid overload and hypoxemia; use of mechanical ventilation also helps clinicians adequately manage pain and agitation without risking respiratory compromise. The SSC guidelines recommend lung-protective strategies in patients requiring mechanical ventilation, including smaller tidal volumes (6-8 mL/kg) and airway pressure release ventilation or high-frequency oscillatory ventilation, in order to maintain oxygenation while minimizing barotrauma.[5] These strategies may require additional sedation and possibly neuromuscular blockade to be effective.

Nurses need to be aware of the potential for decreased venous return secondary to increased intrathoracic pressures that may require additional BP support. While the patient is intubated and mechanically ventilated, nurses should continue to follow protocols to avoid ventilator-associated pneumonia, including maintaining the head of bed at 30 to 45 degrees (unless contraindicated) and following oral care guidelines. Nurses also play a crucial role in determining readiness for extubation.[6]

Sedation and analgesia

A sedation goal should be established at the beginning of treatment using input from the patient (if appropriate), family, and healthcare team. There are no recommendations for drug choice in pediatric patients with sepsis, although dexmedetomidine and etomidate

The literature supports the involvement of the patient and family in the care plan in order to improve outcomes.

should be avoided due to potential sympathetic nervous system inhibition, which could lead to hemodynamic instability.[5] Also, long-term propofol administration in children under age 3 isn't recommended because of the association with life-threatening metabolic acidosis.[5]

Nurses have a crucial role in determining sedation goals, assessing the patient's level of sedation, and titrating sedation as indicated. Maximizing effective sedation will decrease the patient's oxygen requirements and support ventilation.

Glycemic control

Hyperglycemia is associated with negative outcomes such as increased length of stay and even death in pediatric patients in the ICU.[5] Tight glycemic control with blood glucose levels of 180 mg/dL or less is recommended for septic pediatric patients as well as adults. If an insulin infusion is indicated, nurses should perform frequent blood glucose monitoring at regular intervals and infuse a dextrose-containing solution simultaneously due to the high risk of hypoglycemia in the youngest children.[5]

Diuretics/RRT

Fluid overload is a concern with septic patients who've received large-volume fluid resuscitation. RRT is indicated in patients with diuretic-refractory fluid overload. The evidence suggests that patients with less fluid overload before RRT have improved outcomes.[5]

Nutrition

The guidelines recommend parenteral nutrition in children who can't tolerate enteral nutrition.

Psychosocial considerations

In the ICU, nurses have the opportunity to fully assess the patient and interact with the patient's family. For pediatric nursing care, patient and family-centered care is the gold standard. The literature supports the involvement of the patient and family in the care plan in order to improve outcomes. Also, because the proportion of children with chronic health issues who present in sepsis is higher than that of children who have no underlying condition, obtaining a thorough health history is crucial.[9]

Follow the guidelines

A study examining outcomes for adult patients in hospitals that complied with the SSC guidelines showed a statistically significant decrease in mortality.[14] Although this may or may not translate into the pediatric population, it provides an interesting platform for future research. As this article shows,

while a vast amount of research and literature is available regarding the treatment of pediatric sepsis, the opportunities for continued investigation are innumerable. As research progresses, nursing practice must remain current to provide patients with interventions based on the strongest evidence available. ■

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