Fluid Resuscitation in Sepsis

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Objectives

• After completion of this module, participants will:
  – Describe the initial therapy for fluid resuscitation in patients with sepsis and septic shock
  – Compare crystalloid and colloid therapy for fluid resuscitation
  – Identify the risk factors of fluid resuscitation
  – Describe techniques for intravascular volume assessment

New Definitions

Sepsis
• Life-threatening organ dysfunction caused by a dysregulated host response to infection
  – Defined by qSOFA + SOFA scores
  – Emphasizes organ dysfunction
  – De-emphasizes nonspecific systemic inflammation
  – No more "severe sepsis"

Septic shock
• Persistent hypotension requiring vasopressors AND lactate > 2
  • A subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
  – Hypotension + MAP < 65
  – Combination of ↓ BP and ↑ lactate:
    » Significantly higher risk-adjusted mortality for combo (42.3%) vs. for pressures alone (30.1%), lactate > 2 alone (30.7%)


The Ebb and Flow of Sepsis

Complications

Ebb Phase
Optimal Fluid Maintenance
Flow Phase
De-resuscitation

Resuscitation Fluids

<table>
<thead>
<tr>
<th>Solution</th>
<th>Volume expansion* (%)</th>
<th>Duration of volume expansion (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride 0.9%</td>
<td>20-25</td>
<td>1-4</td>
</tr>
<tr>
<td>Lactated Ringer's/PlasmaLyte</td>
<td>20-25</td>
<td>1-4</td>
</tr>
<tr>
<td>5% Albumin</td>
<td>70-100</td>
<td>12-24</td>
</tr>
<tr>
<td>25% Albumin</td>
<td>300-500</td>
<td>12-24</td>
</tr>
</tbody>
</table>

* Expressed as a percentage of administered volume


2016 Sepsis and Septic Shock Initial Management

1. Measure lactate
2. Obtain blood cultures prior to antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30 mL/kg crystalloid for hypotension or lactate of ≥ 4 mmol/L
5. Apply vasopressors (not respond to fluid) -Goal MAP > 65
6. Persistent hypotension despite fluid or ↑ lactate
   - Measure CVP
   - Measure ScvO2
7. Re-measure lactate if initial lactate was elevated

**Initial Resuscitation**

- Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).

- We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).

- We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS).

**Intravascular Volume Assessment**

- We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis (BPS).

- We suggest that dynamic over static variables be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence).

- We recommend an initial target mean arterial pressure (MAP) of 65 mmHg in patients with septic shock requiring vasopressors (strong recommendation, moderate quality of evidence).

- We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (weak recommendation, low quality of evidence).

**Ongoing Fluid Therapy**

- We recommend that a fluid challenge technique be applied where fluid administration is continued as long as hemodynamic factors continue to improve (BPS).

- We recommend crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis and septic shock (strong recommendation, moderate quality of evidence).

- We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis and septic shock (weak recommendation, low quality of evidence).

- We suggest using albumin in addition to crystalloids for initial resuscitation (weak recommendation, low quality of evidence).

**Too Much Fluid is Too Much...**

- Studies suggest that continued fluid therapy after initial fluid resuscitation is harmful
  - Retrospective review (n=350) of fluid resuscitation in septic shock
    - A more positive fluid balance at 24 hours is suggestive of increase mortality, 42% vs 56% (HR 1.519 (1.353 – 1.681))
  - Prospective study (n=50) evaluated fluid boluses over 3 days after initial resuscitation
    - Cumulative fluid balance was associated with worsening SOFA scores, lung injury scores, & PaO2/FiO2 ratio

**The Case Against Too Much Fluid**

- Positive fluid balance associated with worse outcome
  - Prospective, observational trial using SOAP network
  - 3147 patients with ALI

<table>
<thead>
<tr>
<th>Serum LDH (IU/L)</th>
<th>Non-survivors (n=239)</th>
<th>Survivors (n=153)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher fluid volume</td>
<td>90 (68.2)</td>
<td>88 (54.4)</td>
<td>0.619</td>
</tr>
<tr>
<td>Higher plateau pressure</td>
<td>23 (14.3)</td>
<td>25 (16.3)</td>
<td>0.619</td>
</tr>
<tr>
<td>Fluid balance</td>
<td>1.0 ± 2.6</td>
<td>1.0 ± 2.6</td>
<td>0.08</td>
</tr>
<tr>
<td>48 hr</td>
<td>1.7 ± 6.1</td>
<td>2.0 ± 6.6</td>
<td>0.002</td>
</tr>
<tr>
<td>72 hr</td>
<td>1.5 ± 6.0</td>
<td>2.3 ± 6.6</td>
<td>0.002</td>
</tr>
<tr>
<td>16 hr</td>
<td>1.6 ± 6.0</td>
<td>2.3 ± 7.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Median daily</td>
<td>-0.8 ± 1.1</td>
<td>0.9 ± 1.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>-3.0 ± 17.8</td>
<td>0.6 ± 25.6</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>


**Fluid and Outcomes**

- Fluid overload is an independent risk factor for increased mortality and morbidity in critically ill patients

- Fluid overload increases reintubation rate and AKI

- Fluid-conservative approach improves ventilator-free and ICU-free days in patients with ARDS

Fluid Resuscitation

- Early aggressive resuscitation in severe sepsis may improve outcomes
- Normalization of lactate is associated with improved outcomes
- Over aggressive continued resuscitation may do more harm than good
- Crystalloids as the initial fluid of choice
- Albumin can be used when patients require substantial amounts of crystalloids
- Avoid starches and gelatins in sepsis and septic shock

Interprofessional Education Module to Learn, Teach, and Optimize the Treatment of Sepsis

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- Renee Dixon, MD
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- Samuel A. Tisherman, MD
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