Septic Shock: Which Fluid Should I Use?

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Erin Gordon, MD
Pulm/CC Medicine UCSF

Disclosures

• I have no commercial or other interests relevant to this presentation.

Background

• Sepsis is the body’s inflammatory response to infection
• Severe sepsis occurs when this response leads to organ dysfunction or tissue hypoperfusion
• Severe sepsis often progresses to shock
  – 1 in 4 patients who present to the ER with sepsis will develop shock despite appropriate antibiotic therapy (Glickman et al, 2010)

Background

• Pathophysiology of septic shock is partially understood:
  – Lactic acid itself prevents arterial smooth muscle constriction
  – Suppression of vasopression release causes low vascular tone
  – Endothelial nitric oxide production results in arterial vasodilation
Background

- Fluids in conjunction with antibiotics and vasopressors are the mainstay of therapy for septic shock
- Fluids can restore optimal tissue perfusion by expanding the intravascular volume
- Two main questions remain:
  - What is the optimal amount or timing of fluid?
  - What is the optimal fluid to administer?

Options for Fluid Therapy

- Crystalloids: nonbuffered vs buffered
  - Nonbuffered: normal saline
  - Buffered: Lactated Ringers
- Colloids: hypo vs hyperoncotic
  - Hypo-oncotic: 5% albumin
  - Hyper-oncotic: dextrans, starches, 25% albumin
- Red blood cell transfusion

Crystalloids

- Crystalloids include hypo/iso/hypertonic solutions
- Either buffered (Lactated Ringers) or nonbuffered (normal saline)
- Pros:
  - Readily available in virtually any location
  - Inexpensive
- Cons:
  - May be more likely to leak into extravascular space

Colloids

- Hypo-oncotic or hyperoncotic solutions:
  - 5 or 25% albumin
  - Starches
  - Detrans/gelatins
- Pros:
  - Theoretically less likely to leak into extravascular space
  - Possible benefit in sepsis
- Cons:
  - More expensive than crystalloid
  - May be less readily available
  - May have untoward effects on immune function/organ function that are not fully elucidated
  - Starches have been associated with worse mortality and renal dysfunction (NEJM, 2008)
Red Blood Cells

• Pros:
  – Theoretically can improve tissue oxygenation
  – Fluid of choice in massive hemorrhage

• Cons:
  – Expensive
  – May not be readily available
  – Likely has significant effects on immune function and organ function

So which fluid is best in sepsis?

1. Albumin in sepsis (CCM, 2011)
2. Crystalloid vs colloid (JAMA, 2013)
3. Buffered vs nonbuffered crystalloid (CCM, 2014)
4. Lower vs higher transfusion threshold (NEJM, 2014)

The role of albumin as a resuscitation fluid for patients with sepsis: A systematic review and meta-analysis® Critical Care Medicine, 2011

Anthony P. Delaney, MD, FOCM; Alina Dan, MD, FOCM; John McCaffrey, MD, FOCM; Simon Finfer, MD, FOCM

• Background: In 2004, the SAFE trial was published in the NEJM.
  – It compared 4% albumin to normal saline for fluid resuscitation in a heterogeneous group of patients in the ICU
  – No difference in mortality but improved mortality in the prespecified subgroup with severe sepsis.
• Methods: Meta-analysis of albumin vs saline for sepsis
• Results: 17 studies randomized 1977 subjects with sepsis to albumin or other fluid

Slight benefit for the use of albumin in sepsis even after removing the largest trial (SAFE).
**Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock**

The CRISTAL Randomized Trial  
*JAMA, 2013*

- RCT at 57 sites: 2857 patients with hypovolemic shock were randomized to colloid (dextran, starch or albumin) vs crystalloid (saline or LR)
- No difference in mortality, renal dysfunction
- More vent free days in the colloid group

**Conclusion #1**

- Probably no difference in outcome for colloid vs crystalloid in hypovolemia or sepsis
- Colloids may reduce days on ventilator (less fluids administered)
- Starches probably worsen renal function

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**Association Between the Choice of IV Crystalloid and In-Hospital Mortality Among Critically Ill Adults With Sepsis**  
*CCM 2014*

- Multicenter prospective cohort study of 53,448 patients with sepsis (nonsurgical)
- Propensity scoring to match patients and compared balanced vs nonbalanced crystalloid.
- Few patients received only balanced fluids so the % of balanced fluids were calculated
- 6.5% of the subjects received SOME balanced fluids.
- Comparing all subjects: those that received balanced fluids were younger (64 vs 68), received more volume (7 vs 5 L), more likely to get steroids, colloid, invasive monitoring and mechanical ventilation; less likely to have heart failure or renal failure.

Then 3, 365 patients receiving SOME balanced fluids were propensity matched 1:1 to those receiving NO balanced fluids.
- Lower in hospital mortality (19.6 vs 22.8)
- No difference: ARF, ICU stay

Conclusion #2
- Balanced fluid may be associated with reduced mortality in sepsis but this needs to be confirmed in RCT. However, these fluids are readily available and generally considered low risk of adverse effects.
- This association of balanced fluids with mortality has never been described in sepsis but has been seen in operative literature.

- Multicenter RCT of 998 with septic shock and Hg<9 randomized to transfusion threshold of 9 vs 7.
- Excluded ACS, life threatening bleeding, acute burn
Conclusions

1. No difference in mortality for colloid vs crystalloid in hypovolemia or sepsis. Colloids/albumin may result in less volume and more ventilator free days. Starches worsen renal function.
2. Balanced crystalloids (LR) may be associated with improved mortality in severe sepsis. Needs further study.
3. Lower transfusion threshold (7 vs 9) is safe in severe sepsis.

Conclusion #3

• Lower transfusion threshold is safe in patients with severe sepsis.