Albumin: Weighing the Risks and Benefits in Critically Ill Patients

The Value of Albumin

Surgical Grand Rounds

August 13, 2007

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What is Albumin?

- Naturally occurring plasma protein
- Derived from pooled human plasma
- No risk of disease transmission—heated and sterilized by ultrafiltration
- Commonly available in 4%, 5%, 20%, and 25% (5% and 25% in the US)

What Does Albumin Do?

- 4% albumin—slightly hypooncotic
- 5% albumin
  - isooncotic
  - 500 mL expands plasma volume 490 mL or 750 mL
- 20% and 25% albumin
  - Hyperoncotic
  - 100 mL of 25% albumin increases intravascular volume by ~450 mL hypooncotic

Fluid Resuscitation: Crystalloid vs. Colloid

- **Crystalloid**
  - Lactated Ringer’s
  - Normal Saline

- **Colloid**
  - Albumin—safest but most expensive
  - Hydroxyethyl starches
    - Can cause coagulopathy and bleeding complications
    - Can cause renal insufficiency or renal failure
  - Gelatins
    - Produced from bovine collagen
    - Can also cause renal impairment or allergic reaction ranging from pruritis to anaphylaxis
  - Dextran
    - Glucose polymers synthesized by *Leuconostoc mesenteroides* bacteria
    - Risk of renal injury and anaphylactoid reactions

Landmark Albumin Studies

- Cochrane Trials
  - 2000
    - 30 study meta-analysis
    - 1419 patients
    - 6% increase in absolute risk of death in patients receiving albumin
  - Subsequent 55-trial meta-analysis
    - 3504 patients
    - no significant increase in risk of death

Landmark Albumin Studies

- SAFE Study
  - 2004—conducted in Australia/New Zealand
  - Multi-center (16 ICUs)
  - randomized, double-blind trial
  - 4% albumin (slightly hypooncotic) versus 0.9% normal saline
  - Endpoint—28-day rate of death from any cause

SAFE Study (Continued)

- Patient population EXCLUDED ICU admits after cardiac surgery, after liver transplantation, or for the treatment of burns
- Both medical and surgical ICU patients were included in the study

SAFE Study (Continued)

Outcome showed no significant difference in survival times between the albumin and normal saline groups.

SAFE Study (Continued)

- Only significant difference in trauma patients
  - Relative risk of death in albumin group versus normal saline group 1.36
  - Difference due to greater number of patients with trauma AND an associated brain injury who died after random assignment to albumin group
  - No difference in relative risk of death among trauma patients WITHOUT associated head trauma

Benefits of Albumin

- Stays intravascularly for 4-5 hours
- Decreases pulmonary edema/lung injury in aggressive fluid resuscitation
- Increases cardiac output and oxygen delivery
- Improves organ function in critically ill hypoalbuminemic patients
- Increases oncotic pressure in transplanted patients who have lost autonomic nervous system intervention—minimal research on transplanted patients
Lung Injury in Trauma/Hemorrhagic Shock (T/HS) Resuscitation

- 60 experimental rats divided into 3 groups
  - Rats undergoing laparotomy without shock (T/SS)
  - Rats with T/HS and resuscitation with blood plus twice the volume of shed blood as Ringer’s Lactate (RL)
  - Rats with T/HS and resuscitation with blood plus additional 3 mL of 50 g/L human albumin (5%)

Lung Injury in Trauma/Hemorrhagic Shock (T/HS) Resuscitation

- Expression of PMN CD11b/CD18 and intercellular adhesion molecule-1 (ICAM-1) of jugular vein measured
- Severity of lung injury determined by measuring lung tissue myeloperoxidase (MPO) and lung injury score (LIS) after 3 hour recovery period

Lung Injury in Trauma/Hemorrhagic Shock (T/HS) Resuscitation

- Concluded that toxic factors released and produced by post-ischemic intestine in T/HS can be bound by albumin to prevent organ injury


<table>
<thead>
<tr>
<th>Group (n)</th>
<th>CD11b/CD18 (%)</th>
<th>ICAM-1 (U/mL)</th>
<th>MPO (U/g)</th>
<th>LIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>T/SS (20)</td>
<td>17.76 ± 2.11</td>
<td>258.76 ± 98.23</td>
<td>2.53 ± 0.11</td>
<td>-</td>
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<tr>
<td>T/HS + RL (20)</td>
<td>31.25 ± 3.48</td>
<td>356.23 ± 65.6</td>
<td>4.63 ± 1.31</td>
<td>2.62 ± 0.23</td>
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<tr>
<td>T/HS + albumin</td>
<td>20.36 ± 3.21^c</td>
<td>301.01 ± 63.21^c</td>
<td>4.26 ± 1.12^c</td>
<td>1.25 ± 0.24^c</td>
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<td>(20)</td>
<td></td>
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<tr>
<td><em>F</em></td>
<td>6.25*</td>
<td>5.86*</td>
<td>6.26*</td>
<td>-</td>
</tr>
</tbody>
</table>

ICAM-1: Intercellular adhesion molecule-1; MPO: Myeloperoxidase; LIS: Lung injury score. *P < 0.05 vs T/SS group; ^P < 0.05 vs T/HS + RL group; ^P < 0.05 comparison among the three groups (ANOVA).
Greater Cardiac Index and Oxygen Delivery by Albumin than LR in Sepsis

- 28 anesthetized, invasively monitored, and mechanically ventilated female sheep
- Received 0.5g/kg body weight feces into abdominal cavity inducing peritonitis
- Resuscitated with either continuous LR alone, combined with 20% albumin (volume ratio to LR 1:10) or 6% HES (volume ratio to LR 1:1), or gelatin alone
- No antibiotics or vasoactive drugs were administered
- Animals monitored until their spontaneous death

Greater Cardiac Index and Oxygen Delivery by Albumin than LR in Sepsis

Improves Organ Function in Critically Ill Hypoalbuminemic Patients

- Prospective, controlled, randomized study
- 100 patients randomized
  - Half receive 300mL of 20% albumin on the first day and then 200mL/day if serum albumin concentration <31g/dL
  - Other half received no albumin but LR instead
- Primary outcome measure was effect of albumin on organ function by a Sequential Organ Failure Assessment (SOFA) score
- Mean fluid gain almost 3x higher in control
- Albumin gave better tolerance to enteral feeds

Improves Organ Function in Critically Ill Hypoalbuminemic Patients

- Meta-analysis of cohort studies and controlled trials
- 90 cohort studies involving 291,433 patients
- 9 prospective controlled trials with 535 total patients
- Hypoalbuminemia found to be strongly associated with poor clinical outcomes
- Each 10g/L decrease in serum albumin...
  - Increased odds of mortality by 137%
  - Morbidity by 89%
  - Prolonged ICU by 28% and hospital stay by 71%
  - Increased resource utilization by 66%
- Complication rates reduced when serum albumin level exceeds 30g/L

CONCLUSIONS

- Albumin for fluid resuscitation in ICU patients...
  - is appropriate for specific patient populations
  - decreases pulmonary edema/lung injury in aggressive fluid resuscitation
  - increases cardiac output and oxygen delivery
  - improves organ function in critically ill hypoalbuminemic patients
- Better studies need to be conducted for specific patient populations
THANK YOU!