"Small Volume"
Resuscitation for Trauma
Cases : PRO Aspects

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Small Volume Resuscitation: PRO

Lecture Objectives

- Present background for interest in this topic
- Review published studies related to:
  - Crystalloid versus colloid resuscitation
  - Use of hypertonic fluids for resuscitation
    - Determine types of cases where hypertonic resuscitation may be preferable
  - Limiting the volume of preoperative fluids in trauma patients
- Have fun while swaying the audience
"Asanguinous Resuscitation"

Colloid versus Crystalloid

- Metaanalysis of the multiple studies on this indicated 12% improved survival with crystalloid, so general conclusion was that "crystalloid infusion is preferable to colloid for early traumatic shock"
- Advantages of crystalloid:
  - Immediately available and effective
  - Cheaper
  - Nonantigenic
  - May have longer shelf life
- Why haven’t the Europeans paid attention to this?
Background Reasons for Interest in "Small Volume Resuscitation"

- Demonstrated effectiveness of hypertonic sodium solutions for major burn resuscitations, particularly when there was associated closed head injury
  - Less cerebral edema
  - Less tissue edema
  - Less wound complications
  - Quicker return to normal hemodynamics
Background for Military Interest in "Small Volume Resuscitation"

- Weight and volume of standard IV fluids
  - 1 liter plastic bag of normal saline is 2744 cm³ in volume & weighs 1.1 kg
  - So single military medic can only carry enough of this fluid for a limited number of resuscitations
- Also this is a consideration related to the amount of storage space on ground or helicopter ambulances
Early Studies on Hypertonic Saline (HTS) Resuscitation for Trauma

- Used 7.5 % NaCl in 6 % dextran 70 or 5 % glucose (HSD)
  - Contain about 2400 mOsm/liter of sodium chloride
  - The NaCl causes quick increase in mean arterial pressure & cardiac output (at dose of 4 ml / kg), then the dextran maintains these effects longer
  - In animal models enhances overall cardiac efficiency, decreases heart rate & systemic vascular resistance & intracranial pressure
- Potential complications are seizures and myelinolysis from the sodium load, and allergic reactions & bleeding diathesis from the dextran
Summary of Animal Studies Data on HSD Resuscitation for Hemorrhagic Shock

- Immediate increase in systemic pressure & cardiac output
- Peripheral vascular resistance decreased
- Immediate increased central organ blood flow
- Reduced postischemic reperfusion injury
- Increased urinary output
- Reduced gut bacterial translocation
- Increased survival
Results of 1991 Clinical Study of Hypertonic Saline-Dextrose (HSD)

- Multicenter, randomized
- Patients received either 250 cc HSD or 250 cc Normal Saline (NS), then same standard fluids
- Upon E.D. arrival, the HSD group had higher BP, serum osmolality, & serum sodium
- No difference in overall mortality, but HSD patients requiring surgery had better survival & lesser complications than the patients who received NS
- No dextran allergic reactions observed
Two Studies with Favorable Results for HSD Resuscitation


HSD increased the BP of severely injured patients more efficiently than did Lactated Ringer's (LR), and showed tendency toward increased survival in patients with severe head injury.
1994 Metaanalysis Report of Hypertonic Resuscitation

- Metaanalysis of 9 clinical trials with 1889 patients
  - No survival difference between hypertonic saline (7.5 %) alone versus Lactated Ringer's (LR)
  - 5.1 % higher survival with hyperosmolar saline / dextran (7.5 % NaCl / 6 % dextran 70) compared to LR
Cochrane Library Review of HSD Versus Isotonic Crystalloid Resuscitation

- Reviewed 16 trials with 837 patients
- Pooled relative risk of death:
  - 0.84 in trauma patients
  - 1.49 in burn patients
  - 0.62 in patients undergoing surgery
- Conclusions: "Data are insufficient to decide if HSD is better than isotonic crystalloids for resuscitation of trauma, burns, and those undergoing surgery"
Potential Adverse Side Effects Associated with Small Volume Resuscitation

- Hyperosmolar coma
- Hypernatremia
- Hypokalemia
- Seizures
- Dysrhythmias
- Tissue necrosis (if extravasates)
- Hemolysis at injection site
- Anaphylactoid reaction to colloid component
- Coagulopathy if extended use
- Decreased immune function from splenic saturation

However note that these have not been significant in human trials
## Commercially Available Solutions for Small Volume Resuscitation

<table>
<thead>
<tr>
<th>Name</th>
<th>Content</th>
<th>Country Registered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmadex-Hiper</td>
<td>7.5% NaCl, 6% dextran 70</td>
<td>Brazil</td>
</tr>
<tr>
<td>Hiperton</td>
<td>7.5% NaCl, 6% dextran 70</td>
<td>Mexico</td>
</tr>
<tr>
<td>Macrodex HT</td>
<td>7.5% NaCl, 6% dextran 70</td>
<td>Argentina</td>
</tr>
<tr>
<td>Osmohes</td>
<td>7.2% NaCl, 10% HES 200*</td>
<td>Austria</td>
</tr>
<tr>
<td>Tensitron</td>
<td>7.5% NaCl, 6% dextran 70</td>
<td>Czech Republic</td>
</tr>
<tr>
<td>Hyperhes</td>
<td>7.5% NaCl, 6% HES 200</td>
<td>Austria</td>
</tr>
<tr>
<td>Osmohes</td>
<td>7.2% NaCl, 10% HES 200</td>
<td>Hungary</td>
</tr>
<tr>
<td>RescueFlow</td>
<td>7.5% NaCl, 6% dextran 70</td>
<td>Europe</td>
</tr>
<tr>
<td>HyperHAES</td>
<td>7.2% NaCl, 6% HES 200</td>
<td>Germany</td>
</tr>
</tbody>
</table>

* HES = hydroxyethyl starch
## Comparison of RescueFlow & HyperHAES Content

<table>
<thead>
<tr>
<th></th>
<th>RescueFlow</th>
<th>HyperHAES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Electrolyte concentration</strong></td>
<td>7.5 % NaCl</td>
<td>7.2 % NaCl</td>
</tr>
<tr>
<td><strong>Sodium content</strong></td>
<td>1283 mmol / liter</td>
<td>1232 mmol / liter</td>
</tr>
<tr>
<td><strong>Chloride content</strong></td>
<td>1283 mmol / liter</td>
<td>1232 mmol / liter</td>
</tr>
<tr>
<td><strong>Osmolarity</strong></td>
<td>2567 mosmol / liter</td>
<td>2464 mosmol / liter</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>3.5 to 7.0</td>
<td>3.5 to 6.0</td>
</tr>
<tr>
<td><strong>Colloid</strong></td>
<td>dextran</td>
<td>hydroxyethyl starch</td>
</tr>
<tr>
<td><strong>Mean molecular weight</strong></td>
<td>70,000</td>
<td>200,000</td>
</tr>
<tr>
<td><strong>Colloid concentration</strong></td>
<td>6 %</td>
<td>6 %</td>
</tr>
<tr>
<td><strong>Colloid osmotic pressure</strong></td>
<td>70 mm Hg</td>
<td>36 mm Hg</td>
</tr>
<tr>
<td><strong>Container volume</strong></td>
<td>250 ml.</td>
<td>250 ml.</td>
</tr>
</tbody>
</table>
Studies Related to Military Interest in Small Volume Resuscitation

- Single dose of HSD just as effective as IV route if given by intraosseous route
- Intraosseous insertion technique (sternal or ankle) easy to learn by military first responders
- No major tissue damage if single dose HSD used
- New intraosseous drill gun by VidaCare has made the procedure even easier to perform
Is HSD Useful for Resuscitation of Patients with Pulmonary Contusion?

- Porcine study with no change in wet to dry lung weights or CT scan injury volume.
- Concluded: "hypertonic saline resuscitation did not alter pulmonary contusion lesion size, oxygenation, or lung compliance."
- Limited human clinical studies show no HSD benefits for oxygenation or physiologic shunt.
- (Oops, this is actually a CON slide)
Use of Hypertonic Saline for Traumatic Brain Injury (reviewed in *J Trauma* 2001; 50: 367-383)

- 11 human trials have been reported for HST for ICP control
  - Various concentrations used (1.7% to 29.2%)
  - Most did not report comparative mortality
    - One showed increased mortality with HTS continuous infusion & one showed decreased mortality
  - Bolus doses were effective at reducing ICP even in patients who had failed other methods
- Reviewed the 4 reports & one metanalysis of HTS in resuscitation & concluded: "systemic hemodynamics are improved with HTS, & mortality benefits have been shown in a subgroup of patients with TBI & hypotension, likely from the ability of HTS to restore MAP without increasing ICP"
Recent Austrian Observational Study of HSD in Prehospital Trauma Patients

- For this study "Ethics Committee approval was not required"
- Used Hyperhes (6 % HES & 7.5 % NaCl)
- 100 patients; 11 deaths within 24 hours (11 %)
- Showed improvements in median BP, HR, & O2 saturation at hospital arrival
- However other fluid Rx was not controlled:
  - 75 % of cases received colloids
  - 99 % received 1 to 1.5 liters LR
Recent Australian Report on Prehospital Hypertonic Saline Use

Cooper et al., *JAMA* 2004; 291 (11): 1350-1357.

- Double-blind, prospective, randomized trial
- Prehospital cases entered Dec. 1998 to April 2002 in Melbourne, Australia
- Case entry criteria:
  - Coma due to blunt head trauma (GCS < 9)
  - Hypotension (systolic BP < 100)
- Patients with multisystem trauma excluded
- Patients received either 250 cc 7.5 % saline (HTS) or 250 cc LR, then more LR and/or Haemacell colloid at the discretion of the paramedics
Results and Conclusions of the Australian Prehospital HTS Study

- 229 patients enrolled
- Demographics similar between the 2 groups, except:
  - HTS group received average of 500 cc colloid versus 250 cc in the control (LR) group
  - Both groups received average of 1250 cc more fluid
  - No statistically significant difference in survival (trend though toward higher survival in HTS group (55 % versus 47 % at 6 months)
- No difference in BP at hospital arrival (120 systolic in both groups), hospital length of stay or neurologic outcome (functional status at discharge and at 6 months)
Unique Aspects Reported in a Recent Military Review Article *(J Trauma 2003; 54: S52-62)*

- Noted that 250 cc hypertonic saline (without dextran) (HTS) is roughly equivalent to 2 liters of Normal Saline.
- Reported their animal studies that showed HTS resuscitation was effective in dehydrated animals but caused a high % of local soft tissue complications if given intraosseously (bone marrow necrosis and compartment syndrome); this has not been seen in human trials.
- Mentioned future possibility of using freeze-dried plasma which could be reconstituted with a small volume of fluid.
  - Long shelf life.
  - Could be made in advance for soldiers using their own plasma.
  - They did not cite any study references on this however.
The Controversy Over Prehospital IV Fluid Treatment for Trauma

- Main article supporting concept of "delayed fluid resuscitation (or “permissive hypotension”) for hypotensive patients with penetrating torso injuries" (to prevent alleged increased bleeding from clot displacement due to fluid resuscitation):
  - Bickell W.H. et al.
  - Prospective, randomized
  - Cases from Houston, Texas, 1989 to 1992
  - 309 immediate IV fluid resuscitation patients
    - 62 % survived
  - 289 delayed resuscitation patients
    - 70 % survived
Problems with the "Delayed Fluid Resuscitation" Study

- Only a few small scale supportive animal studies (one of these used 80 ml/kg LR started 6 minutes after aortotomy)
- Change in either group of 4 or 5 deaths would have altered the statistical outcome
- Calculated probability of survival was 3 % less in the immediate group
- Results only apply to penetrating truncal trauma (not blunt) and short prehospital times
Study Comparing "Delayed Resuscitation" with Hypertonic Saline / Dextran


- Measured blood loss after spleen injury in dogs
  - Two groups received no fluid resuscitation
  - One group received 33 ml/kg LR over 15 min.
  - One group received 4 ml/kg of 7.5% NaCl / 6% dextran over 4 minutes

- Measured blood loss same in all groups
- Groups not receiving fluid had progressive low flow state with declining cardiac output (progressive shock)
Could HSD be Used for "Permissive Hypotension"? (see *J Trauma* 2003; 54: S43-45)

- Only a couple of animal studies have looked at this
- Volume of HSD required to maintain BP of 70 mm Hg in animals bleeding from an aortotomy was < 10% the volume of LR required
- However "it is not known whether permissive hypotension would worsen the incidence of late complications that could arise from incomplete resuscitation. In addition, evidence would suggest that resuscitation to a systolic BP of 80 mm Hg would be inadequate to improve cerebral perfusion after head injury".
Small Volume Resuscitation: PRO

Lecture Summary

- **Crystalloid** is generally preferable to **colloid** for most trauma resuscitations.

- **Limiting the volume of preoperative resuscitation fluid** may be appropriate for some cases of penetrating trunk trauma with internal bleeding.

- **Hypertonic saline resuscitation** can be a useful temporizing measure for some field and combined injury (i.e., burns or hypotension with closed head injury) situations, but cannot yet be recommended as a standard routine technique for most trauma cases.

- More human studies on this are needed.