Fluid Resuscitation in the Critically Ill...

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Choosing the Right Solution

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“Two drachms of muriate and two scruples of carbonate, of soda, to sixty ounces of water”
History

- 1834: First use of albumin
- 1876: Sidney Ringer
- 1876: Alexis Hartmann adds lactate
Fluid Resuscitation

- One of the most common interventions
  - Maintain hydration
  - Correct hypovolemia
  - Improve tissue oxygenation
Fluid Resuscitation

• Selection based on:
  ‣ Geography
  ‣ Specialty (medical vs. surgical)
  ‣ Hospital

• Left to the most junior physician
Fluid Resuscitation

- Dosing and timing important

- Selection of IVF may affect patient-centered outcomes
Crystalloid vs. Colloid
Fluids are Drugs
Acid-Base Effects
Acid-Base

• Primary effect is to alter acid-base status

• Final acid-base equilibrium of IVF:
  ✓ Strong ion difference (SID)
  ✓ Concentration of nonvolatile weak acids
  ✓ $P_aCO_2$
Acid-Base

- Primary effect is to alter acid-base status
- Final acid-base equilibrium of IVF:
  - Strong ion difference (SID)
  - Concentration of nonvolatile weak acids
  - $P_a\text{CO}_2$
SID

- Net charge of fully dissociated cations ($\text{Na}^+$, $\text{K}^+$, $\text{Ca}^{2+}$, $\text{Mg}^{2+}$) and anions ($\text{Cl}^-$, lactate, ketoacids)

- $[\text{Strong cations}] - [\text{Strong anions}]$

- Normal SID $\approx 40$ mEq/L
• Lower than plasma $\text{HCO}_3^-$ = pH ↓

• Higher than plasma $\text{HCO}_3^-$ = pH ↑
The Ideal Solution

• Normotonic
• SID ≈ 24 mEq/L
• No ancillary cations
• Uses bicarbonate in preference to bicarbonate substitutes
Crystalloid vs. Colloid
“There’s nothing normal about normal saline”
Normal Saline

- Not a true physiologic solution
  - Na: 154 mEq/L
  - Cl: 154 mEq/L
  - pH: 5.0
  - Osmolarity: 308 mOsm/L
  - SID = 0

Hyperchloremic Metabolic Acidosis
Is NS Harmful?

- Chloride concentration
  - 40% higher than plasma
  - Increases systemic inflammation
  - Renal vasoconstriction and decline in GFR
  - Greater likelihood of RRT
Is NS Harmful?

- Emerging Literature...
  - Renal
  - Pulmonary
  - Splanchnic
  - Circulatory
  - Coagulation
Is NS Harmful?

• Observational study

• Adult patients

• 0.9% NS vs. Plasma-Lyte in patients undergoing major abdominal surgery
Major Complications, Mortality, and Resource Utilization After Open Abdominal Surgery

0.9% Saline Compared to Plasma-Lyte

- **32,000** patients
  - Saline: 30,994
  - Plasma-Lyte: 926
Mortality

- Saline: 5.6%
- Plasma-Lyte: 2.9%

RRT, transfusions, postop infection all greater with NS
Prospective, open-label, before-and-after

22 bed ICU in Melbourne, Australia

Chloride restrictive strategy associated with a decrease in AKI?
Control period

- 0.9% NS
- 4% gelatin
- 4% albumin in NS
• Intervention period
  ▪ Lactated crystalloid (Hartmann’s)
  ▪ Plasma-Lyte 148
  ▪ Cl “rich” solutions could be given in pts with hyponatremia, cerebral edema
Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

- **1533 patients**
  - 760 in control
  - 773 in intervention
● Results
  ▪ **Lower increase** in creatinine
  ▪ **Decreased incidence** of “injury” and “failure” according to RIFLE
  ▪ **No change in mortality**
• Limitations
  ‣ Not blinded or randomized
  ‣ Observation bias
  ‣ Changed outcomes from trial registration
  ‣ Composite endpoints
  ‣ Lots of solutions
“There’s nothing normal about normal saline”
Crystalloid vs. Colloid
Balanced Solutions
Balanced Solutions

- Must lower SID in parallel with dilution of weak acids

- Exact balance with SID of 24 mEq/L
  - Assuming normocarbia
  - Saline would be balanced by replacing 24 mEq/L chloride with HCO$_3^-$
  - Bicarbonate not included in IVFs
Balanced Solutions

- Achieve lower Cl⁻ concentrations by adding organic anions
  - L-lactate
  - Acetate
  - Gluconate
  - Citrate
Balanced Solutions

• Add ancillary cations
  ✓ K+
  ✓ Ca^{2+}
  ✓ Mg^{2+}
Balanced Solutions

- Trials
Prospective, randomized, double-blind

DKA patients - LSU Shreveport

NS vs. Plasma-Lyte A
45 patients
- 23 to NS
- 22 to P-Lyte

Plasma-Lyte resulted in higher $\text{HCO}_3^-$ and lower $\text{Cl}^-$ concentrations
Randomized, double-blind, parallel-group

Single-center in California

Does Plasma-Lyte A better correct base deficit at 24 hrs after injury
46 patients

- GCS 9
- Penetrating injury to head, neck, chest, abdomen
- SBP < 90 mm Hg
- Need for intubation or OR
- Within 60 min of arrival
Results

- Base deficit corrected to normal in 6 hrs with Plasma-Lyte group

- Arterial pH corrected to normal by 6 hrs in Plasma-Lyte group
Balanced Solutions

- Solutions
  - Plasma-Lyte
  - Isolyte
  - Lactated Ringer’s
  - Hartmann’s
Plasma-Lyte A

- Contents
  - Na: 140
  - Cl: 98
  - K: 5
  - Mg: 3
  - Acetate: 27
  - pH: 7.4
  - Osmolarity: 294
  - SID: 50
Lactated Ringer’s

- Contents
  ✓ Na: 130
  ✓ Cl: 109
  ✓ K: 4
  ✓ Ca: 2.7
  ✓ Lactate: 28
  ✓ pH: 6.5
  ✓ Osmolarity: 274
  ✓ SID: 28
Crystalloids

- Normal Saline
  - Not physiologic
  - SID = 0
  - Hyperchloremic metabolic acidosis

- Balanced Solutions
  - Plasma-Lyte (SID = 50)
  - Lactated Ringer’s (SID = 28)
Crystalloid vs. Colloid
Colloids
Albumin

• Available since 1940s
  ✓ 4% - 5% solution: roughly iso-oncotic
  ✓ 20% - 25% solution: hyperoncotic
Albumin

- Healthy patients
  - 4% - 5% expands volume by amount almost equal to volume infused
  - 20% - 25% expands by 4-5 times volume
  - 90% retained 2 hrs after infusion

- Retention much less in disease states
Albumin

- Cochrane Injuries Group Albumin Review
  - Systematic review
  - Effects of albumin on hypovolemia, burns
  - 32 trials (1200 patients)
  - Mortality
    - Albumin: 16.4%
    - Non-albumin: 9.5%
Albumin

- SAFE Trial (2004)
  - 16 academic, tertiary centers in Australia and New Zealand
  - Compare 4% albumin to NS
  - All-cause mortality
Albumin

- SAFE Trial (2004)
  - 6997 patients
  - No difference in mortality
  - Severe sepsis subgroup
    - 1218 patients
    - Adjusted OR for death 0.71
Albumin

- SAFE Trial (2004)
  - 6997 patients
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  - Adjusted OR for death 0.71
Albumin

- Severe sepsis / septic shock
  - ✓ 5% solution
  - ✓ Adjunct to crystalloids

- SBP
  - ✓ 25% solution
  - ✓ 1.5 g/kg within 6 hrs of diagnosis
Colloids
HES

- Approximately 6 million pts/year
- Characterized by:
  - Molecular weight
  - Degree of hydroxyethylolation
- New generations
  - Lower weights (130 kDa)
  - Lower substitution ratios
798 patients

Mortality

- 51% in HES group
- 43% in Ringer’s group
- RR 1.17
- Number need to harm 13
Assessment of hemodynamic efficacy and safety of 6% hydroxyethylstarch 130/0.4 vs. 0.9% NaCl fluid replacement in patients with severe sepsis: The CRYSTMAS study

- Prospective, multicenter, double-blind, randomized
- 6% HES vs. 0.9% NS
- 196 patients with severe sepsis
  - Trend towards more RRT and higher mortality with HES
Prospective, blinded RCT

32 centers in Australia / New Zealand

6% HES vs. 0.9% NS
• 7000 patients

• Mortality
  ‣ HES: 18%
  ‣ NS: 17%
  ‣ RR 1.21 for RRT in HES group
Limitations

- Excluded patients unlikely to survive
- Included elective surgical patients
- Lower mortality than expected
• Multicenter, randomized trial
• 57 ICUs in France, Belgium, Canada, Algeria, and Tunisia
• Colloids vs. crystalloids for fluid resuscitation in critically ill
2857 Patients

- No prior fluids during ICU stay
- Required fluids for acute hypovolemic shock
- Crystalloids
  - Isotonic or hypertonic saline
  - Buffered solutions
2857 Patients

- No prior fluids during ICU stay
- Required fluids for acute hypovolemia
- Colloids
  - Hypooncotic (4% or 5% albumin)
  - Hyperoncotic (HES, 20-25% albumin)
Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock
The CRISTAL Randomized Trial

- **Mortality - 28 days**
  - Colloid: 25.4%
  - Crystalloid: 27%
- **No increase in RRT in colloid group**
Limitations

- Non-blinded
- Took 9 years to recruit
- Enrolled in ICU
- 20% of colloid group got crystalloids
- Poor randomization: groups different
Should no longer be used in the critically ill
Choosing the Right Solution...

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Crystalloid vs. Colloid
Take Home Points

• No definitive evidence of superiority

• Selection of IVF should receive same degree of scrutiny as medications

• Acid-base equilibrium

  ✓ Strong ion difference
Take Home Points

- Normal Saline
  - Not a true physiologic fluid
  - Supraphysiologic concentrations of Cl
  - SID = 0
  - Hyperchloremic metabolic acidosis
Take Home Points

- Plasma-Lyte
  - SID = 50
  - Alkalinizing solution
  - Better for pre-existing acidosis?
Take Home Points

- **Lactated Ringer’s**
  - ✓ SID = 28
  - ✓ Osm = 274
  - ✓ Caution in hyponatremia, cerebral edema
  - ✓ Incompatible with PRBC infusion
Take Home Points

- **Albumin**
  - ✓ Severe sepsis / septic shock
  - ‣ 5% solution
  - ‣ Adjunct to crystalloid
  - ✓ SBP
  - ‣ 25% solution
  - ‣ 1.5 g/kg within 6 hrs
Take Home Points

- HES
  ✓ Should no longer be used in critically ill patients
“This being my first case, I fancied my patient secure, and from my great need for a little repose, left her in charge of the surgeon; but I had not been gone long, ere the vomiting and purging recurring, soon reduced her to a state of debility...”
“I was not appraised of the event, and she sunk in five and a half hours after I left her. As she had previously been of sound constitution, I have no doubt the case would have resulted in complete reaction, had the remedy, which had already produced such an effect, been repeated.”
Thank You!

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For additional EM/Critical Care discussions, go to:
ccpem.com
“Having inserted a tube into the basilic vein, cautiously-anxiously, I watched the effects; ounce after ounce, but no visible change was produced. Still persevering, I though she began to breath less laboriously, soon the sharpened features, and sunken eye, and fallen jaw, pale and cold, bearing the manifest of death’s signet, began to glow with returning animation...
the pulse, which had long ceased, returned to the wrist; at first small and quick, by degrees it became more and more distinct, fuller, slower, and firmer; when six pints had been injected, she expressed in a firm voice that she was free from all uneasiness; her extremities were warm and every feature bore the aspect of comfort and health”