COLLOIDS VS CRYSTALLOIDS IN FLUID RESUSCITATION OF CRITICALLY ILL PATIENTS

DR. PRATEEK VERMA (ANAESTHETICS)
The various Fluids

Physiology and Pathophysiology of Fluid Distribution

Role of various fluids in critically ill patients
HISTORY

• 1832 – Dr. Thomas Latta used intra-venous Saline for the first time

• 1834 – Dr. John Mackintosh used intra-venous Albumin for the first time

• 1876 – Sidney Ringer introduced the Ringer’s solution

• 1885 – Alexis Hartmann modified Ringer’s solution to include Lactate and used it for rehydration of children with gastro-enteritis

• 1941 – development of blood fractionation and use of Albumin in large quantities for resuscitation of patients burned in the Pearl Harbor attack
**INTRA-VENOUS FLUIDS**

**COLLOIDS**
- A homogeneous non-crystalline substance consisting of large molecules or ultramicroscopic particles of one substance dispersed through a second substance
- Can NOT pass freely through the capillary membrane

**CRYSTALLOIDS**
- A substance that, when dissolved, forms a true solution
- Can pass freely through the capillary membrane
COLLOIDS

NATURAL - Albumin

SYNTHETIC

Dextran

Gelatins

Starches

Dextran 40

Dextran 70

Cross-linked Gelatins/Oxypolygelatins (ex-Gelofundiol)

Urea cross-linked Gelatin (ex-Haemacell)

Succinylated Gelatins/Modified Fluid Gelatins (ex-Gelofusine)

1st generation - Hetastarch

2nd generation - Pentastarch

3rd generation – Tetrastarch, Voluven, Venofundin

4th generation - Tetraspan
PHYSIOLOGY OF FLUID DISTRIBUTION

Extracellular space = 45% of body water

ICS: Intracellular space 55% of body water
ISS: Interstitial space

I.V. Fluids

STARLING EQUATION

REVISED STARLING EQUATION
REVISED STARLING EQUATION

\[ J_v = K_f \left( [P_c - P_i] - \sigma [\pi_c - \pi_s] \right) \]

- \( J_v \) – net filtration
- \( P \) – hydrostatic pressure
- \( \pi \) – oncotic pressure
- \( K_f \) – filtration co-efficient
- \( \sigma \) – reflection co-efficient

The Endothelial Surface Layer (ESL) is formed mainly by the Endothelial Glycocalyx (EG) and this excludes a small area known as the Subglycocalyx. The subglycocalyx has a much lower protein concentration as compared to the capillary blood and thus the gradient opposes outward filtration.
Forces opposing filtration are NEVER greater than the forces favoring filtration

There is NO ABSORPTION at the venous end

The fluid lost to the interstitium is returned back to the circulation via the Lymphatics

“The concept of giving a colloid to ‘suck’ fluid back into the vasculature is a MYTH”

- Paul Ellis Marik

**TRADITIONAL MODEL OF FLUID EXCHANGE**

- \( P_c \gg P_i \)
- \( \pi_c \gg \pi_i \)

**REVISED MODEL – NO ABSORPTION**
DISTRIBUTION OF COLLOIDS

1000 ml

IVS 20%

ECS ≈ 33%

EVS 80%

ICS ≈ 66%
DISTRIBUTION OF CRYSTALLOIDS

- 1000 ml
- 800 ml (EVS 80%)
- 200 ml (IVS 20%)

- ECS ≈ 33%
- ICS ≈ 66%
PATHOPHYSIOLOGY OF FLUID DISTRIBUTION IN CRITICAL ILLNESS

- Trauma
- Systemic Inflammation
- Sepsis
- Surgery
- Volume Overload
- Diabetes
Damaged glycocalyx, less tight junctions

Colloids distribute between the Intravascular and Interstitial compartments

More edema formation

Reduced efficacy of volume expansion

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>PATIENTS</th>
<th>COLLOID : CRYSTALLOID</th>
<th>RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAFE</td>
<td>ICU</td>
<td>Albumin : NS</td>
<td>1 : 1.4</td>
</tr>
<tr>
<td>VISEP</td>
<td>Severe Sepsis</td>
<td>HES : RL</td>
<td>1 : 1.3</td>
</tr>
<tr>
<td>CHEST</td>
<td>ICU</td>
<td>HES : NS</td>
<td>1 : 1.8</td>
</tr>
<tr>
<td>6S</td>
<td>Severe Sepsis</td>
<td>HES : Ringer’s acetate</td>
<td>1 : 1</td>
</tr>
<tr>
<td>CRISTAL</td>
<td>Sepsis, Trauma</td>
<td>Colloids : Crystalloids</td>
<td>1 : 1.5</td>
</tr>
<tr>
<td>ALBIOS</td>
<td>Severe Sepsis</td>
<td>Albumin : Crystalloids</td>
<td>1 : 1</td>
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</table>
ROLE OF VARIOUS FLUIDS IN RESUSCITATION OF CRITICALLY ILL PATIENTS
HUMAN ALBUMIN (HA)

• MW – 69000 Da
• **Commercially available HA** – 4% HA (hypo-oncotic)
  - 5% HA (iso-oncotic)
  - 20% and 25% HA (hyper-oncotic)
**HUMAN ALBUMIN (HA)**

- **Pharmacokinetics**
  - leads to initial volume expansion (80% with 4% HA and 200-400% with 25% HA)
  - the volume effect lasts for 16 – 24 hours

- **Risks and Side Effects**
  - pulmonary edema
  - impaired coagulation and hemostasis
  - electrolyte and acid-base disturbances – hyperchloremia, as it is prepared in NaCl solution
  - immunologic reactions – HA is generally well tolerated, but immediate allergic reactions characterized by fever, nausea, vomiting, pruritus, hypotension and even cardio-vascular collapse are possible
<table>
<thead>
<tr>
<th>YEAR</th>
<th>TRIAL</th>
<th>CONCLUSIONS</th>
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<tbody>
<tr>
<td>1998</td>
<td>Cochrane Injuries Group Albumin Reviewers (CIGAR)</td>
<td>Administration of Albumin was associated with a significant increase in the rate of death - caused significant alarm (Study population – patients with hypovolemia, burns or hypoalbuminemia)</td>
</tr>
<tr>
<td>2004</td>
<td>Saline vs Albumin Fluid Evaluation (SAFE)</td>
<td>In patients in the ICU, use of either 4% Albumin or Normal Saline for fluid resuscitation results in similar outcomes at 28 days</td>
</tr>
<tr>
<td>2011</td>
<td>Fluid Expansion As Supportive Therapy (FEAST)</td>
<td>Questioned the role of BOLUS fluid resuscitation with either Albumin or Saline in critically ill patients (rate of death: bolus therapy with either &gt;&gt;&gt; no bolus therapy)</td>
</tr>
<tr>
<td>2014</td>
<td>ALBumin Italian Outcome Sepsis (ALBIOS)</td>
<td>In patients with sepsis, Albumin replacement in addition to crystalloid, as compared with crystalloid alone, did not improve the rate of survival at 28 and 90 days</td>
</tr>
<tr>
<td>2015</td>
<td>Lactated Ringer versus Albumin in early sepsis therapy (RASP)</td>
<td>No difference in primary (30-day mortality) or secondary (ICU mortality, ICU and hospital length of stay, 90-day mortality, daily SOFA score, rates and length of mechanical ventilation, renal replacement, needing of vasopressor) outcomes</td>
</tr>
<tr>
<td>Current</td>
<td>PRECISE, EARRS</td>
<td></td>
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A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

The SAFE Study Investigators*

- Blinded, RCT
- 4% Albumin vs 0.9% Saline for intravascular fluid resuscitation
- 6697 patients admitted ICU’s in Australia and New Zealand
<table>
<thead>
<tr>
<th>BENEFICIAL</th>
<th>NEUTRAL (NO SIGNIFICANT DIFFERENCE)</th>
<th>HARMFUL</th>
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</table>
| Resuscitation with Albumin was associated with a decrease in the adjusted risk of death at 28 days in patients with severe sepsis (sub-group analysis) | • Rate of death at 28 days *(primary outcome)*  
• Length of ICU stay  
• Length of hospital stay  
• Duration of Mechanical Ventilation  
• Duration of Renal Replacement Therapy  
• Rate of new organ failure | Resuscitation with Albumin was associated with a significant increase in the rate of death at 2 years among patients with Traumatic Brain Injury (no difference in patients with trauma without brain injury) |

CONCLUSIONS

In patients in the ICU, use of either 4 percent albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.
INDICATIONS

Absolute:

1. Paracentesis - >5L or >5g albumin/L in ascitic fluid
2. Therapeutic Plasmapharesis – plasma exchange > 20ml/kg
3. Spontaneous Bacterial Peritonitis in Cirrhosis – associated with antibiotic administration

Relative:

1. Cirrhosis – diuretic-resistant ascites with albuminemia < 2g/dL
2. Hemorrhagic shock – only when not responsive to crystalloid and synthetic colloids
3. Hepatorenal syndrome – in association with vasoconstrictors
4. **Nephrotic syndrome** – in the presence of albuminemia < 2g/dL associated with hypovolemia and/or pulmonary edema

5. **Burns** - > 30% of the body surface area, after the first 24 hours

6. **Organ transplantation** – in the presence of albuminemia < 2g/dL and PCV>30%, in post-operative liver transplant patients, in order to control ascites and peripheral edema

7. **Major surgery** – only if albuminemia < 2g/dL and after the restoration of normovolemic

8. **Cardiac surgery** – third choice after crystalloids and synthetic colloids
# HYDROXY-ETHYL STARCHES

<table>
<thead>
<tr>
<th>BENEFICIAL</th>
<th>NO BENEFIT</th>
<th>HARMFUL</th>
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</thead>
<tbody>
<tr>
<td>CRISTAL study (Colloids vs Crystalloid)</td>
<td>• CHEST trial (HES vs NS) [2012]</td>
<td>• 6S trial (HES vs Ringer’s acetate) [2012]</td>
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<td></td>
<td>• Bagshaw et al (HES vs NS) [2013]</td>
<td>• Zarychanski et al [2013]</td>
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<td>• Serpa Neto et al [2014]</td>
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<tr>
<td></td>
<td>• Rochwerg et al [2014]</td>
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</table>
Hydroxyethyl Starch 130/0.42 versus Ringer’s Acetate in Severe Sepsis

• a/k/a 6S – Scandinavian Starch for Severe Sepsis/ Septic Shock trial

• Blinded, RCT

• 6% HES (130/0.42) vs Ringer’s Acetate up to a dose of 33ml/kg of ideal body weight

• Patients with Severe Sepsis
Results – HES was associated with

- Increased rate of death or dependent on dialysis at 90 days (primary outcome)
- Increased requirement of Renal Replacement Therapy
- Increased risk of bleeding
- Decreased percentage of days alive without Renal Replacement Therapy and out of the hospital
- No difference in incidence of other secondary outcomes
ANY CHOICE AMONG CRYSTALLOIDS ???

CHLORIDE-LIBERAL VS CHLORIDE-RESTRICTED

0.9% SALINE

BALANCED SALT SOLUTIONS (BSS)
Effect of aBuffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit: The SPLIT Randomized Clinical Trial

- Blinded, RCT
- Plasmalyte-148 vs 0.9% Saline [SPLIT - Saline vs PlasmaLyte for ICU fluid Therapy]
- Patients admitted to ICU requiring crystalloid fluid therapy

CONCLUSIONS AND RELEVANCE: Among patients receiving crystalloid fluid therapy in the ICU, use of a buffered crystalloid compared with saline did not reduce the risk of AKI. Further large randomized clinical trials are needed to assess efficacy in higher-risk populations and to measure clinical outcomes such as mortality.
The use of 0.9% Saline has been associated with:

- Hyperchloremic metabolic acidosis
- Decreased renal blood flow
- Renal cortical hypoperfusion
THE FINAL STATEMENT

Consensus Statement by the ESICM and Cochrane umbrella:

- **Colloids** – no clear benefit of colloids (expensive) over crystalloids (inexpensive)
  - overall show increased mortality in patients with Traumatic Brain Injury (TBI)

No indications currently exist for the use of colloids over crystalloids

- **Albumin** – no unique benefit as a resuscitation fluid
  - no mortality benefit in sepsis
  - high cost and limited shelf-life

Use of Albumin as a resuscitation fluid is not supported
• **Hydroxy-Ethyl Starches (HES)** – no proven benefit
  - associated with increased harm (AKI, need for Renal Replacement Therapy, coagulopathy and need for blood transfusion)
  - no consensus on safe dose

  Use of HES in resuscitation should be avoided

• **Gelatins and Dextrans** – not well studied
  - no evidence of harm or benefit
  - theoretical potential for adverse effects

  Suggestion is not to use Gelatins or Dextrans
• **0.9% Saline** – hyperchloremic metabolic acidosis
  - decreased renal blood flow
  - renal cortical hypoperfusion

  Superseded by Balanced Salt Solutions (BSS), especially in high risk populations [ex – increased risk of AKI, diabetic ketoacidosis]

• **Balanced Crystalloid Solutions/BSS** – have shown no adverse effects in any particular patient population
  - evidence of benefit over NS by avoiding hyperchloremic metabolic acidosis

  Current literature supports the use of BSS when possible (no consensus exists on a single preferred solution), and in particular in patients in which NS may cause adverse effects
TAKE HOME POINTS

• Fluids should be administered with the same caution that is used with any intravenous drug.

• Fluid resuscitation is a component of a complex physiological process.

• Fluid requirements change over time in critically ill patients.

• Specific considerations apply to different categories of patients.

• NO IDEAL RESUSCITATION FLUID EXISTS.
Thank you