Algorithmic Quantification of Prime and Perfusate Composition to Regulate Physiological Variables during Cardiopulmonary Bypass in Neonates and Infants

Isaac Chinnappan, MS CCP LCP FPP CPBMT
Monroe Carell Jr. Children’s Hospital at Vanderbilt
October 4, 2018

Objectives

- How to calculate variables of fluid dynamics to keep prime and perfusate in near normal physiologic phase
- Review of routine prime components, Essential Ratio’s of the prime, Efficacy of Pre-BUF, Breakdown of Total Body Water
- PRBC’s, FFP and ATIII
- Bidirectional Fluid loss/Wastage and impact on COP

Objectives

- Sodium Bicarbonate:
  - Identify Acidic Biomarkers
  - pH stat and normal ranges of PCO2 during profound hypothermic perfusion
  - Lactate clearance
**Variables**

**Hemodilution**

**Non-Hemic Dilution**

**Hemic Variables**

**Non-Hemic Variables**

- Colloid Osmotic Pressure
- Isotonicity
- Anion Gap
- Sodium
- AT III
- Lactate

---

**Non-Hemic Variables - Circuitry**

- The new concept or Evidence Based Clinical Practice recommends:
  - Reduction of static volume and Maintenance of fluid consistency
  - Even very less “CIRCUITRY REDUCTION” matters positively

**Hemic Variables - Circuitry**

- FFP
- PRBC’s

---

**Non Hemic Variables - Circuitry**

- How to define a small or a big baby
- Reducing of static volume and Maintenance of fluid consistency
- Even very less “CIRCUITRY REDUCTION” matters positively

**Hemic Variables - Circuitry**

- FFP
- PRBC’s

---

**Non-Hemic Variables**

- Circuit: Minimal Safe Required (Size:Length:Flow)
CPB - Circuit

- Circuit Characteristics
  - Miniaturized circuits
  - To accommodate forward and return flow
  - Def: The smallest possible circuit that can accommodate the required forward and return flow with appropriate size cannulae

I. Prime and Perfusate Composition

Prime or Perfusate Composition

- Isotonic solution (Plasmalyte A, Normosol-R, etc.)
  - Not much variation in clinical practice
- Mannitol (Dosing - Not much variation in clinical practice)
- pRBC - Huge variation with reference target HCT
  - In the prime
  - During CPB at different hypothermic phases

Prime or Perfusate Composition-cont.

- Albumin (25%)
- FFP (+/-) – Huge variation in dosage and timing of administration
- Calcium – AABB recommendations!??
  - Per AABB - 250mg/unit of PRBC
- Sodium Bicarbonate – Concerns in assessing acidic biomarkers and required/need/preferred administration
Description of the Topic

- During CPB in Neonates and Infants:
  - How much we need to treat an abnormal variable
  - How to calculate/to measure/to estimate
  - More Physiological Fluid and flow Dynamics (prime and perfuate) is essential to achieve Homeostatic Hemodynamics

Homeostatic Hemodynamics

- Fluid composition or consistency or dynamics at all phases of CPB
- Very important during fluid addition
- This reflects on Function (Heart and the Lung)

Prime Composition

- Isotonic Solution (Plasmalyte-A or Normosol-R)
- PRBC’s: Acceptable or adequate post-dilutional HCT
- +/- FFP (Dosage and Recommendation = Huge Variation)
- Isotonicity (Osmolarity)
- Oncotiity – Amount of Albumin 25% (Huge Variation)
- Calcium (AABB Recommendation)
- Mannitol and Acceptable or adequate Heparin
- Sodium Bicarbonate

“In Pediatric Cardiac Surgery you cannot too gentle and you cannot too accurate”.

- Dwight McGoon, MD
Essential Ratio’s of THE PRIME

• With reference Patient’s weight
• Ratio 1: Baseline - RBC:Plasma (Patient’s)
• Ratio 2: Prime: pRBC:FFP
• Ratio 3: Post-dilutional HCT: pRBC:FFP
• Ratio 4: [Heparin]:Total Priming Volume
• Ratio 5: COP:Albumin 25%
• Ratio 6: Calcium: Priming Volume
• Ratio 7: Isotonicity of the Total Priming Volume

Additional Variables

• Pre-BUF the circuit volume
• Physiologic Blood Gas of the prime(when?)
• Anion gap
• Lactate, Na, K, HCO₃, Anion Gap and Glucose levels
  • What happens after sometime or just before going on CPB)
  • In summary: (= Hemic + Non-Hemic + Isotonic + Oncotic)

Additional Variables

• Pre-BUF the circuit volume
• Pre-BUF: The Pre-BUF effluent volume to be removed should be in a 3:1 ratio to the volume of PRBC’s added to the ECC (If PRBC is 200ml, the Effluent volume should be ~600ml)
• Sodium, Glucose, Potassium, Anion gap, HCO₃ and Lactate levels
• Physiologic Blood Gas of the prime

II. Breakdown of Total Body Water
Breakdown of Total Body Water

<table>
<thead>
<tr>
<th>Adult (70Kg)</th>
<th>Infant (5Kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Body Weight</td>
<td>60%</td>
</tr>
<tr>
<td>Extracellular</td>
<td>40%</td>
</tr>
<tr>
<td>Intracellular</td>
<td>20%</td>
</tr>
<tr>
<td>Plasma</td>
<td>10%</td>
</tr>
<tr>
<td>Interstitial</td>
<td>5%</td>
</tr>
<tr>
<td>Interstitial</td>
<td>5%</td>
</tr>
</tbody>
</table>

Total Volume

Adult

- % Body Weight: 60%
- Extracellular: 40%
- Intracellular: 20%
- Plasma: 10%
- Interstitial: 5%
- Intestinal: 5%

- Total Volume: 42L

Infant

- % Body Weight: 70%
- Extracellular: 40%
- Intracellular: 30%
- Plasma: 15%
- Interstitial: 5%
- Intestinal: 25%

- Total Volume: 3.5L

III. pRBC

Blood Prime

<table>
<thead>
<tr>
<th>Weight Kg</th>
<th>Units Transfused</th>
<th>Received Transfusion</th>
<th>Target HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 – 10</td>
<td>2+1</td>
<td>100</td>
<td>35 – 40</td>
</tr>
<tr>
<td>11 – 15</td>
<td>1+1</td>
<td>70</td>
<td>30 – 35</td>
</tr>
<tr>
<td>16 – 20</td>
<td>0+1</td>
<td>15</td>
<td>25 – 30</td>
</tr>
<tr>
<td>11 – 15</td>
<td>NIL</td>
<td>55</td>
<td>25 – 30</td>
</tr>
<tr>
<td>16 – 20</td>
<td>0+1</td>
<td>7</td>
<td>25 – 30</td>
</tr>
<tr>
<td>16 – 20</td>
<td>NIL</td>
<td>93</td>
<td>25 – 30</td>
</tr>
</tbody>
</table>

Composition of pRBC

- RBC - Total mL? AABB: Per unit of PRBC: ~250-350mL
- Most often it's around 280mL
- AABB: 15mL of CPD per 100mL of PRBC [1.5mL / 10mL]
- CPD in 280mL of pRBC is around 42mL
- HCT around 60% [Range 58 – 62%]
- pRBC volume: 168mL (if the actual total volume 280mL)
**Priming CPB circuit**

- High glucose in bank blood
  - > 500 mg%
  - Increased osmolarity
  - High glucose damages hypoxic brains
- Acidic bank blood
  - Add Na HCO3
  - Increased osmolarity
  - Na > 145 mEq/L damages kidneys & brains

CPB prime and preBUF to achieve more physiologic perfusate

**Prime Osmolarity Calculation**

- If Na = 140mEq/L and Glucose = 70mg/dl
  - 2Na + Glucose \(- I\) = 350mOsm.L\(^{-1}\)
  - 2Na + Glucose/18 – II = 284mOsm.L\(^{-1}\)
  - (Na x 2) + (Glucose/18) + 15 – III = 299mOsm.L\(^{-1}\)
- Either formula II or III is acceptable
- Higher glucose beneficial in maintaining Normo-Osmolarity

**Blood Chemistry in Prime**

<table>
<thead>
<tr>
<th>Prime</th>
<th>pH</th>
<th>pCO2 mmHg</th>
<th>pO2 mmHg</th>
<th>Na mEq/L</th>
<th>K mEq/L</th>
<th>GLU mg/dl</th>
<th>LAC mmol/L</th>
<th>HCT %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC Not Washed</td>
<td>&lt; 6.80</td>
<td>129</td>
<td>27</td>
<td>129</td>
<td>16</td>
<td>&gt;500</td>
<td>18.4</td>
<td>60</td>
</tr>
<tr>
<td>PRBC Cell Saver Washed</td>
<td>&lt; 6.80</td>
<td>11</td>
<td>37</td>
<td>142</td>
<td>1.8</td>
<td>189</td>
<td>2.7</td>
<td>63</td>
</tr>
<tr>
<td>Reconstituted WB Prime No Pre-BUF</td>
<td>7.38</td>
<td>43</td>
<td>558</td>
<td>159</td>
<td>6.1</td>
<td>301</td>
<td>5.6</td>
<td>23</td>
</tr>
<tr>
<td>PRBC Prime/Pre-Buf</td>
<td>7.40</td>
<td>44</td>
<td>163</td>
<td>152</td>
<td>3</td>
<td>59</td>
<td>1.6</td>
<td>35</td>
</tr>
<tr>
<td>Baseline</td>
<td>7.47</td>
<td>31</td>
<td>121</td>
<td>135</td>
<td>3.6</td>
<td>102</td>
<td>0.8</td>
<td>35</td>
</tr>
</tbody>
</table>

**Isotonic and Oncotic Imbalance**

- **Isotonic Imbalance:**
  - Fluid shift in and out of cells
- **Oncotic Imbalance:**
  - Extracellular (INTRAVASCULAR) and Interstitial fluid shift leads to edema and eventual organ failure
IV. FFP

Composition of FFP

We analyzed 35 samples of fresh frozen plasma (FFP), finding mean concentrations of 535 mg/dl glucose, 172 mEq/L sodium, 73 mEq/L chloride, 3.5 mEq/L potassium, 15 mEq/L bicarbonate, and 5.5 g/dl protein with 60% albumin.

Thus, FFP is a hyperosmolal, hyperglycemic, hypernatremic, and hypochloremic solution which may be a less effective volume expander than other albumin containing hypertonic solutions.

FFP in Prime

2011 Update to The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists Blood Conservation Clinical Practice Guidelines

Plasma transfusions share many of the risks and complications associated with RBC transfusions. Therefore, reduction or avoidance of plasma transfusions should be among objectives of blood conservation strategies.
- AT III concentrate is preferred for heparin resistance (20-25% of CPB patients show heparin resistance).
- Prophylactic use of plasma in routine cardiac surgeries is not associated with reduced blood loss or less transfusion requirement, and this practice is not recommended.
- FFP transfusion recommended only for factor deficiency.

Cost Analysis

- FFP:
  - A unit (280-320mL) price: $1,000
- AT III:
  - Price per UNIT: Thrombate III: $4.50 per IU
  - ATryn: $2.34 per International Unit
Cost Analysis

Formula:

Units = Desired %AT III - baseline %AT III x weight

For example: 10 kg

Desired %AT III = 60
Baseline %AT III = 30

Units needed = (60 - 30) x 10

50 units/kg will increase AT III by 30%

Recommended AT III During CPB: 60 - 80% (Below 60% critical)

Formula based administration of AT III is cost effective

Non-Hemic Variable

V. Bidirectional loss/Wastage of COP

Estimate the COP loss

HCT : PLASMA
30% : 70% (1 : 2.3)
25% : 58.5% (70 - 11.5) - I

When you increase HCT back to 30%, PLASMA component drops to 47%
30%:47% (58.5-11.5) – II
Fluid administration from anesthesia – III
While weaning from bypass, loss in the circuit volume - IV

When and How to Measure or Estimate Albumin Redosing during CPB?
Estimate the COP loss

HCT : PLASMA
30% : 70% (1 : 2.3)
25% : 58.5% (70 - 11.5) - I

When you increase HCT back to 30%, PLASMA component drops to 47%
30%:47% (58.5-11.5) – II

If you calculated to maintain 4g/dl of Albumin; after bidirectional loss, it would be ~2g/dl

VI. COP
Remember
bi-directional loss or
4-dimensional loss

VII. Sodium Bicarbonate
Acidic Biomarkers

NaHCO₃
• Are we giving appropriate required correction or overcorrecting the deficit?
• Triggers to add NaHCO₃
  • pCO₂ Levels within physiological limits (Alpha stat and pH stat)
  • Reservoir level, Temperature, HCO₃⁻ - level (Not Deficit)
  • Role of protein buffer (Hemoglobin and Albumin)
  • Role of intra-cellular acidosis
**NaHCO₃**

- Rationalize the administration of sodium bicarbonate during profound hypothermic perfusion (PHP)
- Keeping the acidic-biomarkers (pH, pCO₂, HCO₃ and base deficit) within near normal physiological limits
- Preventing hypernatremia during PHP-CPB in neonates and infants

**pH stat - Normothermic**

<table>
<thead>
<tr>
<th>ACID BASE</th>
<th>pCO₂ STAT</th>
<th>pCO₂ NORMO</th>
<th>pCO₂ Hypothermic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALPHA</td>
<td>35-45</td>
<td>35-45</td>
<td>35-45</td>
</tr>
<tr>
<td>pH</td>
<td>70-75</td>
<td>30-40</td>
<td></td>
</tr>
</tbody>
</table>

**Additional Info**

- **During PH stat:**
  - Administration of NaHCO₃ is inevitable to maintain the pH, HCO₃ and BE within normal limits
  - Literature says NaHCO₃ fails to function as a buffer below 28°C
  - Temperature corrected pCO₂ levels around 40 - 45mmHg causing the perfusate to be hypercarbic and acidic requiring more NaHCO₃

**How to Treat Base Deficit**

- In the prime
- During CPB
- During profound hypothermic CPB
- pH Stat; base deficit correction sodium levels
- pH Stat; range of pCO₂ to prevent hypercarbic influenced acidosis
**Modifications – Acidic Biomarkers**

<table>
<thead>
<tr>
<th>PH stat</th>
<th>PCO2 mmHg</th>
<th>Temp</th>
<th>PCO2 mmHg</th>
<th>Temp Not - Corrected</th>
<th>ETCO2 mmHg</th>
<th>HCO3 mEq/L</th>
<th>BE mEq/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTROL GROUP (n = 20)</td>
<td>7.25 – 7.30</td>
<td>40 - 45</td>
<td>80 - 100</td>
<td>35 - 40</td>
<td>28 - 32</td>
<td>-2 to +2</td>
<td></td>
</tr>
<tr>
<td>STUDY GROUP (n = 20)</td>
<td>7.35 – 7.40</td>
<td>30 - 35</td>
<td>60 - 70</td>
<td>30 - 33</td>
<td>20 - 22</td>
<td>Ignored</td>
<td></td>
</tr>
</tbody>
</table>

**NaHCO3 – ABM – Na - Osmolality**

<table>
<thead>
<tr>
<th>PH</th>
<th>PCO2 mmHg</th>
<th>Temp Corrected</th>
<th>PCO2 mmHg</th>
<th>Temp Not - Corrected</th>
<th>ETCO2 mmHg</th>
<th>HCO3 mEq/L</th>
<th>BE mEq/L</th>
<th>Na mEq/L</th>
<th>Osmolar Moles/Lit</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTROL GROUP (n = 20)</td>
<td>7.25 – 7.30</td>
<td>40 - 45</td>
<td>80 - 100</td>
<td>35 - 40</td>
<td>28 - 32</td>
<td>-2 to +2</td>
<td>153±15</td>
<td>354±8</td>
<td></td>
</tr>
<tr>
<td>STUDY GROUP (n = 20)</td>
<td>7.35 – 7.40</td>
<td>30 - 35</td>
<td>60 - 70</td>
<td>30 - 33</td>
<td>20 - 22</td>
<td>Ignored</td>
<td>138±13</td>
<td>304±8</td>
<td></td>
</tr>
</tbody>
</table>

**NaHCO3**

- NaHCO3 was administered only after normalizing non-HCO3 variables referred as acidic biomarkers (pCO2, glucose, lactate, anion-gap (COP?) and reservoir volume)
- Didn’t administer if the sodium level was 145mEq/L and above

**IX. Lactate**
Lactate

Internal: Intracellular vs. Extracellular
External: Transfusion

• Three types (Physiologic, Fluid addition and Intracellular)
• Physiologic - Ischemic generated
• Addition: Due to addition of pRBC and Sudden return of cavity volume
• Concerning Impact on the Hemodynamics
• Lactate clearance – Only Perfusionist can do without compromising the perfusate composition

Summary
• Calculate variables of fluid dynamics to keep prime and perfusate in near normal physiologic phase
• Quantification of routine prime components is essential
• Bidirectional Fluid loss/Wastage and impact on COP
• Sodium Bicarbonate: Identify Acidic Biomarkers
• pH stat and normal ranges of pCO2 during profound hypothermic perfusion
• Lactate clearance

Thanks