Pediatric Parenteral Nutrition

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Parenteral Nutrition (PN)

• PN is lifesaving for many pediatric patients
• Associated with complications
  – Immediate
  – Long term
• PN process involves multiple disciplines and professions
• Potential for medication errors
• “High risk” therapy per Institute for Safe Medication Practices (ISMP)

PN and Past Medication Errors

• Deaths in home patients related to Ca/P precipitation and pulmonary emboli
• Death of patient receiving 50% dextrose for 2 days
• Infant deaths related to incorrect dextrose %
• Irreversible brain damage in a neonate receiving PN with no dextrose
• Iron overload and liver toxicity in a child receiving iron dextran via PN

PN and Past Medication Errors

- Infection in children (2 deaths) from contaminated PN
- NICU outbreak related to contaminated IV lipids
- Death of a child receiving high potassium PN at home
- Magnesium toxicity in 2 premature infants related to compounder malfunction
- Death of a preterm infant due to zinc overload/toxicity
- Death of a toddler due to heparin overdose


Fatal 1,000-fold overdoses can occur, particularly in neonates, by transposing mcg and mg.

September 6, 2007

6 week old infant dies after receiving PN with 60 times more sodium than prescribed.

April 11, 2011

Contaminated PN solutions lead to deaths in Alabama hospitals.

April 11, 2011

PN Safety at Le Bonheur

- PN solutions compounded at Le Bonheur
  - also for Methodist Gtown and South NICUs
- CPOE / Abacus software system for PN
- Standardized PN process for Methodist / Le Bonheur system
  - Standard order form
  - Standard limits for pediatric patients

PN Safety at Le Bonheur

- PN additives ordered as amount per kg per day
- Abacus system limits
  - Neonates, peds < 40 kg or > 40 kg
  - Central v. peripheral access
- Multiple double check systems in place
  - Physician to PN Service
  - PN Service to Pharmacy
  - Nursing to PN Service and Pharmacy
Pharmacist writes paper PN order with Physician co-signature

Pharmacist enters PN order into compounder software program; faxes order to pharmacy

IV pharmacist verifies faxed order against compounder order

Second pharmacist verification

PN compounded

IV pharmacist checks compounded PN against paper order, compounder label and compounder report

PN infusion to Patient at 8PM

Nurse checks PN label against paper order prior to infusion

PN infusion to Patient at 8PM

Compounder Limits

- Inherent system limits generally prevent large errors
- Institution specific limits can allow a more specific supplementation range

Le Bonheur System Limits

<table>
<thead>
<tr>
<th>Additive</th>
<th>≤ 1 yr Central</th>
<th>≤ 1 yr Peripheral</th>
<th>Peds ≤ 40 kg Central</th>
<th>Peds ≤ 40 kg Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium per day</td>
<td>40 mEq/day</td>
<td>40 mEq/day</td>
<td>90 mEq/day</td>
<td>90 mEq/day</td>
</tr>
<tr>
<td>Calcium per kg</td>
<td>0.1 mEq/kg</td>
<td>2.1 mEq/kg</td>
<td>3.1 mEq/kg</td>
<td>2.1 mEq/kg</td>
</tr>
<tr>
<td>Calcium per L</td>
<td>46 mEq/L</td>
<td>16 mEq/L</td>
<td>30 mEq/L</td>
<td>16 mEq/L</td>
</tr>
<tr>
<td>Magnesium per kg</td>
<td>0.66 mEq/kg</td>
<td>0.66 mEq/kg</td>
<td>0.66 mEq/kg</td>
<td>0.66 mEq/kg</td>
</tr>
<tr>
<td>Magnesium per L</td>
<td>NA</td>
<td>1.01 mEq/L</td>
<td>1.01 mEq/L</td>
<td>1.01 mEq/L</td>
</tr>
</tbody>
</table>

Le Bonheur System Limits: Zinc

<table>
<thead>
<tr>
<th>Additive</th>
<th>≤ 1 yr Central</th>
<th>≤ 1 yr Peripheral</th>
<th>Peds ≤ 40 kg Central</th>
<th>Peds ≤ 40 kg Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc per day</td>
<td>6.1 mg/day</td>
<td>6.1 mg/day</td>
<td>6.1 mg/day</td>
<td>6.1 mg/day</td>
</tr>
<tr>
<td>Zinc per kg</td>
<td>NA</td>
<td>NA</td>
<td>6.1 mg/kg</td>
<td>6.1 mg/kg</td>
</tr>
<tr>
<td>Zinc per L</td>
<td>0.56 mg/kg</td>
<td>0.56 mg/kg</td>
<td>0.56 mg/kg</td>
<td>0.56 mg/kg</td>
</tr>
</tbody>
</table>
Home PN and Errors

- Dextrose % much lower than prescribed
- Phosphorous and/or calcium removed from PN
- Protein product substitution
- PNs compounded as TNAs with potentially unstable concentrations of base components and additives
- PNs mixed with incorrect dextrose concentration
- Over or under doses prescribed when transcribing to home PN order form
- PN solutions not delivered to home

Discharge on Home PN

- Complicated process
- Multiple disciplines involved
- Potential for errors throughout process
- Need to assess competency of the home care companies
- Plan in place for appropriate follow-up and monitoring
- Initial and periodic review of home PN orders

COMMUNICATION IS KEY TO A SAFE DISCHARGE!!

PN Ordering and Compounding Concepts

To start writing the order

- Fluid rate
  - Maintenance
  - Other losses
    - Gastric
    - Wound
    - Chest tube
- Glucose tolerance
  - Stress
  - Medications (steroids)
  - Disease (pancreatitis)
- Underlying disease
  - Renal failure
  - Liver disease

- Access
  - Peripheral
    - Max peripheral osmolarity (900 – 1000 mOsm/L)
    - Limit dextrose (10 – 12.5%)
    - Limit K (40 mEq/L)
    - Limit Ca (10 – 20 mEq/L)
    - Limit amino acids, Na
  - Not quite CVL
  - CVL
### Fluid (kcal) requirements

- **< 1 - 1.5 kg**: 150 ml/kg
- **1.5 - 2.5 kg**: 120 ml/kg
- **Up to 10 kg**: 100 ml/kg (up to 1000 ml)
- **>10 – 20 kg**: 1000 ml + 50 ml/kg for each kg from 10 – 20 (up to 1500 ml)
- **>20 kg**: 1500 ml + 20 ml/kg for each kg > 20

### Basic Compounding Concepts

- Components available in known concentrations
  - Amino acids (10 – 15%)
  - Dextrose (50 – 70%)
  - Calcium gluconate (~ 0.5 mEq/ml)
  - Electrolytes, vitamins/trace elements, other additives
- Sterile water to make the final volume of solution

### Osmolarity of Parenteral Nutrients

- Amino acids: 100 mOsm / %
- Dextrose: 50 mOsm / %
- Lipids: 1.7 mOsm / %
- Sodium, potassium: 2 mOsm / mEq
- Calcium gluconate: 1.4 mOsm / mEq
- Magnesium sulfate: 1 mOsm / mEq
Example peripheral solution

3 kg infant on peripheral PN (300 ml volume):
- 10 % dextrose 500 mOsm/L
- 2.5% AA 250 mOsm/L
- Na/K (2 mEq/kg each) 80 mOsm/L
- Ca (10 mEq/L) 10 mOsm/L
- Mg (0.4 mEq/kg) 4 mOsm/L

844 mOsm/L

44 kcal/kg/day (not including lipid calories)

Protein

- Preterm infants 3 – 3.5 g/kg/day
- Term infants 2.5 – 3 g/kg/day
- Children 1.5 – 2 g/kg/day
- Adolescents 0.8 – 1.2 g/kg/day
- Increased needs with critical illness
- Limit to 2.5 g/kg/day (infants) with liver disease

Protein and Cysteine

- Pediatric amino acid product + cysteine for infants < 1 year of age
  - Trophamine
  - Premasol
  - Aminosyn PF
- Standard amino acid product for older children
  - Travasol
  - Aminosyn

\[ \text{Gly + Cys + Glu = glutathione} \]

\[ \text{SO}_4 \]

\[ \text{taurine} \]

\[ \text{methionine} \]

\[ \text{S adenosyl methionine (SAMe)} \]

\[ \text{creatinine, choline, carnitine} \]

\[ \text{homocysteine} \]

\[ \text{S adenosyl homocysteine} \]

\[ \text{homocysteine} \]

\[ \text{bili (pyridoxine)} \]

\[ \text{hepatic cystathionase} \]

\[ \text{cysteine} \]

\[ \text{cystine} \]
**Sodium**

<table>
<thead>
<tr>
<th></th>
<th>meq/L</th>
<th>100 ml/kg</th>
<th>75 ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/4 NS</td>
<td>38.5</td>
<td>3.85 meq/kg</td>
<td>2.7 meq/kg</td>
</tr>
<tr>
<td>1/3 NS</td>
<td>51</td>
<td>5.1 meq/kg</td>
<td>2.8 meq/kg</td>
</tr>
<tr>
<td>1/2 NS</td>
<td>77</td>
<td>7.7 meq/kg</td>
<td>5.8 meq/kg</td>
</tr>
<tr>
<td>LR</td>
<td>130</td>
<td>13 meq/kg</td>
<td>9.8 meq/kg</td>
</tr>
<tr>
<td>NS</td>
<td>154</td>
<td>15.4 meq/kg</td>
<td>11.6 meq/kg</td>
</tr>
</tbody>
</table>

Usual dosing: 2 – 4 meq/kg

**Na during AmphiB Therapy**

**Anion with Na and K**

- Mostly use Cl
- Acetate (OAc)
  - Bicarbonate incompatible with PN (Ca & magnesium)
  - Precursor salt (e.g., acetate) converted in vivo to bicarbonate
  - Generally give 0.5 – 1 meq/kg in VLBW neonates
- Phos
  - NaPO₄ preferred over KPO₄ (decreased aluminum content)

**Compounding Issues: Ca and P**

- Calcium and phosphorous solubility dependent on:
  - pH
  - final solution concentrations of each
  - temperature (cold is better)
  - time
- Calcium gluconate preferred salt
  - Dissociates more slowly than calcium chloride (less precipitation)
  - May have more aluminum contaminant (not leaching from glass)
- Ca (mEq/L) + P (mmol/L):
  - ≤ 50 for Trophamine
  - ≤ 30 for Travasol
Percent Dissociation of Ca Gluconate and Ca Chloride


Ca/P Solubility in D10, FreAmine III

Ca/P Solubility in D10, 2.4% TrophAmine with cysteine

IV Fat Emulsion (IVFE)

- Soybean oil based emulsion
- Primarily long chain fat
- Dose:
  - Term and preterm infants: up to 3 g/kg/day
  - Older children: < 30% total calories as fat
  - Liver disease: limit to 1 g/kg/day
Total Nutrient Admixtures (TNA)

- Lipids are negatively charged particles
- Limits to Ca/P/Zn/Mg/Fe additions
- Stability is pH & multivalent cation dependent
- Cannot visualize particulates
- Cannot use 0.2 micron filter (use 1.2 micron)
- Not recommended in infants/children

Standardized PN Solutions

- Also referred to as premixed PN
- Clinimix (amino acids, dextrose, electrolytes)
- Sulfite free, sterile, nonpyrogenic, hypertonic solutions
- 1 and 2 liter dual chamber bags
  - Amino acids with electrolytes
  - Dextrose with calcium
  - Seal must be broken and contents mixed well prior to administration
- For central and peripheral PN administration
- MVI added by the Le Bonheur pharmacy

Clinimix Solutions

- Dextrose 10% with either 2.75% or 4.25% amino acids with electrolytes
- Dextrose 25% with 4.25% amino acids and electrolytes
- Na 35 mEq/L (~ 1/4NS)
- K 30 mEq/L
- Acetate 51 – 70 mEq/L
- Magnesium 5 mEq/L
- Ca 4.5 mEq/L; Phos 15 mmol/L
PN Complications

- Mechanical/technical
- Infections
- Metabolic
- Refeeding syndrome

Long term complications:
- PN associated liver disease
- Metabolic bone disease
- Essential fatty acid deficiency
- Micronutrient deficiency
- Aluminum accumulation

Metabolic Complications

- Hyperglycemia: stress, infection, steroids/other meds, pancreatitis, DM, excessive dextrose
- Hypoglycemia: abrupt dextrose withdrawal, excessive insulin
- Excess CO2 production: excessive dextrose
- Hypertriglyceridemia: stress, infection, familial hypertriglyceridemia, pancreatitis, excessive IVFE, rapid IVFE infusion rate
- Increased liver function tests: stress, infection, excessive carbohydrate/total calorie, EFAG, long term PN
Metabolic Acidosis

- Reasons for metabolic acidosis related to PN solution:
  - Excess amount of acid in the solution
  - Hydrogen ions released by metabolism of nitrogen sources
- Early amino acid products: metabolic acidosis common
  - Amino acids primarily as HCl salts
- Current crystalline amino acid products: metabolic acidosis NOT common
  - Amino acids as free base or as acetate salts

Hyperchloremic Metabolic Acidosis

- Normal anion gap: the primary problem for the acidosis is a decrease in serum bicarbonate
- This is compensated for by an increase in serum chloride ion
- Common causes:
  - Renal loss of HCO3- (RTA, renal failure)
  - GI losses (diarrhea)
- Normal anion gap (cations minus anions)
  - Na (+ K) minus Cl- and HCO3-
  - Normal range approximately 8-16

Long Term Complications

- PN associated liver disease prevention and management
  - Enteral feeding
  - Cycling
  - Ursodiol
  - Do not overfeed
  - Omega 3 fatty acids (fish oil)
- Metabolic bone disease prevention
  - Adequate Ca/P provision
- Micronutrient deficiency/accumulation prevention
  - Monitoring, careful selection of products

Calculations
Counting Parenteral Kilocalories

• Dextrose = 3.4 kcal/g
  (% dextrose × volume = g)

• Fat = 9 kcal/g

<table>
<thead>
<tr>
<th></th>
<th>10% IVFE</th>
<th>20% IVFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat kcal/ml</td>
<td>0.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Glycerol kcal/ml</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Total kcal/ml</td>
<td>1.1</td>
<td>2</td>
</tr>
</tbody>
</table>

• Protein = 4 kcal/g

Example Peripheral Solution: Calories

3 kg infant on peripheral PN (300 ml volume):
• 10% dextrose 102 kcal/day
• 2.5% amino acids 30 kcal/day
  132 kcal/day
• 132 kcal/day divided by 3 kg = 44 kcal/kg/day
  (calculation does not include lipid calories)

Example Calories: Lipids

• Lipids at 1 g/kg/day × 3 kg = 3 g/day
• 3 g ÷ 20 g/100 mL (i.e. 20% emulsion) = 15 mL
• 15 mL/24 hours = 0.625 mL/hr
• Round rate to 0.6 mL/hr × 24 hrs/day = 14.4 mL
• 14.4 mL/day × 2 kcal/mL = 28.8 kcal/day or 9.6 kcal/kg/day