Ensuring Safe Management of Parenteral Nutrition During Drug Shortages:

Strategies and Protocols for Enabling Clinician Success

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nothing to disclose
Objectives

- Discuss the causes of current and recent PN drug shortages
- Outline the RDs role
- Identify professional society resources and guidelines available
- Discuss prioritizing limited supplies to patients with the greatest need
- Provide insight into development of creative protocols and strategies for practical day to day management of PN patients experiencing drug shortages
PN During Shortages

- Lipid Emulsions
- Amino Acids
- Multivitamin
- Trace Elements
  - Multi trace element products
  - Selenium
  - Copper
  - Zinc
  - Chromium
- Electrolytes
  - Calcium gluconate
  - Magnesium sulfate
  - Sodium phosphate
  - Potassium phosphate
  - Potassium chloride
  - Potassium acetate
  - Sodium Chloride
  - Sodium Acetate
- Sterile Ethanol
U.S. Drug Shortages

FDA Center for Drug Evaluation and Research Trends.
Courtesy CAPT. Valerie Jensen, Center for Drug Evaluation and Research (Feb 2011)
Reasons for Sterile Injectable Shortages

- Product quality issues: 54%
- Discontinuations: 11%
- Delays/capacity: 21%
- Raw material: 5%
- Loss of manufacturing site: 3%
- Component problems/shortages: 2%
- Increase demand due to another shortage: 4%

Adapted from Jensen, FDA CDER. ISMP 2011
Legislation

• Preserving Access to Life-Saving Medication Act (H.R. 2245/S. 296)

• Drug Shortage Prevention Act (H.R. 3839)

• Signed into law July 2012

• Food and Drug Administration (FDA) Safety and Innovation Act (FDASIA)

• New requirements on manufacturers for early notification of issues that could lead to a potential shortage or disruption in supply
RD Role

• Assess all patients receiving PN for appropriateness and ability to transition to enteral nutrition

• Knowledge of signs and symptoms of electrolyte, vitamin, and trace element deficiencies

• Recommend timeframe for increased monitoring of laboratory values

• Suggest supplementation, enteral alternatives, and adjustments to PN additives

• Prioritize limited supplies for patients with the greatest need based on nutritional requirements and gastrointestinal anatomy
Professional Resources

A.S.P.E.N
www.nutritioncare.org

American Society of Health System Pharmacists

www.ashp.org/shortages

FDA

Ensuring Clinician Success

• Ensure clinicians/staff have access to professional guidelines

• Know the patient population to determine reasonable alternatives

• Establish competencies
  • I.e. clinicians aware of s/s micronutrient/trace deficiencies, pros & cons of enteral supplementation, etc.

• Staying abreast of upcoming shortages as a manager & communicating with staff & medical team
Ensuring Clinician Success

- Planning ahead
  - Establishing protocol for dealing with potential PN drug shortages BEFORE they occur

- Involving clinicians in the planning/development

- Communicate with the interdisciplinary team

- Frequent re-evaluation of the protocol
  - What is working?
  - What is not?
  - Patient population specific
Intravenous Fat Emulsion (IVFE)

- Inpatient setting
  - Adult on PN for less than 2 weeks
    - NO IVFE
  - Adults on PN greater than 2 weeks
    - 100 grams of IVFE weekly

- Long term home PN (HPN)
  - 100 grams of IVFE weekly
  - example: 500 mL of 20% IVFE once weekly

If NO IVFE available (NPO/malabsorption of oral fat)
- soybean or safflower oil to arms/legs BID
- triene:tetraene ratio for EFAD

A.S.P.E.N. Information to use in the event of an intravenous fat emulsion shortage, 2010
Amino Acids (AA)

- 10% AA shortage
  - Change AA brands based on availability of other products

- 15% AA shortage
  - Reduce protein delivery temporarily
  - Increase volume as able and change to 10% AA
  - Limit to volume restricted patients only

- Premix PN?
Multivitamin (MVI)

- Inpatient setting
  - MVI to 5 mL dose daily

- Long term HPN
  - Limit MVI to 3x week, full 10 mL dose
  - Patients actively being weaned to enteral nutrition
    - D/c MVI, start chewable vitamins orally / via feeding tube

A.S.P.E.N. Multivitamin Shortage Plan, 2012
Multivitamin (MVI)

- All MVI supplies are exhausted:
  - Individual PN vitamin entities
    - Daily:
      - Thiamine 6 mg
      - Vitamin C 200 mg
      - Folate 0.6 mg
      - Pyrioxine 6 mg
    - Weekly
      - IV Vitamin K 5-10 mg
    - Monthly
      - Cyanocobalamin 1000mcg

A.S.P.E.N. Multivitamin Shortage Plan, 2012
Trace elements

• Multi trace element (MTE) packages
  • MTE 4  MTE 5  3 mL dose
  • MTE 4C MTE 5C 1 mL dose

• Single nutrient admixtures
  • Copper  Zinc
  • Manganese  Selenium
  • Chromium
Trace Elements

• Multi trace element (MTE) shortages
  • Inpatient:
    • Reduce dose in half
    • Discontinue MTE for patients tolerating partial enteral nutrition
    • Provide single trace element supplements (zinc, copper, chromium, selenium, manganese) if no MTE available

• Long term HPN
  • Provide full dose MTE 3 times weekly
  • Discontinue MTE if tolerating partial enteral nutrition
  • Discontinue MTE if HPN is being actively weaned from PN
Trace Elements

- Copper
  - Copper gluconate
  - serum copper < 70mcg/dL
    - 2 mg TID copper gluconate PO
  - serum copper 70-85 mcg/dL
    - 2 mg BID copper gluconate PO

- Chromium
  - Daily multivitamin with mineral supplement PO

- Manganese
  - Deficiency rare, supplementation therefore not required

- Zinc
  - Zinc sulfate or zinc chloride can be added to PN
  - 220 mg Zinc Sulfate PO orally if existing zinc deficiency
  - *Copper & Zinc enteral interaction
    - Competition for enteral absorption

- Selenium
  - Use MTE5 or MTE 5c (has 60 mcg of Selenium)
  - Reduce 120 mcg to 60 mcg to ration
  - 200 mcg Selenium PO daily BID
Electrolytes

- Calcium
- Magnesium
- Phosphorus
- Potassium
- Sodium
Calcium Gluconate

• Inpatient
  • Omit calcium from short term PN
  • Monitor ionized calcium levels (serum calcium is protein bound)
    • If ionized calcium is low
      • Supplement with IV calcium chloride outside the PN bag in acute care setting
    • *Calcium chloride and calcium gluconate dose not equivalent
    • (3x more calcium per 1 gram of Calcium chloride vs. 1 gram of calcium gluconate)
    • Calcium Chloride should not be used in PN solutions due to lack of stability data with calcium chloride

• Long term HPN
  • Reduce calcium gluconate from 15 to 5 mEq in long-term HPN patients to conserve
  • When no calcium, omit and monitor ionized calcium levels
Magnesium

- Inpatient
  - Minimize use Magnesium sulfate while maintaining normal serum values
  - If no Magnesium sulfate, substitute Magnesium chloride in PN solutions
    - grams magnesium sulfate = grams of magnesium chloride
- Long term HPN
  - If no Magnesium sulfate, substitute Magnesium chloride in PN solutions
    - If no Magnesium chloride available
      - Magnesium lactate (Mag tab) PO
      - Avoid magnesium oxide PO due to laxative effect
    - Ensure RDs communicate this to medical team
Magnesium

- Magnesium Lactate (Mag tab) Dosing

<table>
<thead>
<tr>
<th>Serum Magnesium (mg/dL)</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>1.5</td>
<td>3 tabs nightly</td>
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<tr>
<td>1.2 – 1.5</td>
<td>1 tab after meals, 3 tabs nightly</td>
</tr>
<tr>
<td>&lt; 1.2 (if not symptomatic)</td>
<td>2 tabs 1 hour after meals, 3 tabs nightly</td>
</tr>
</tbody>
</table>

1 g Magnesium Sulfate = 8 mEq
1 gram Magnesium sulfate = 98 mg elemental Magnesium
MagTab SR (magnesium lactate) 84 mg elemental Magnesium = 7 mEq magnesium
Phosphorus

• Sodium or potassium phosphate shortages
  • Switch between sodium phos or potassium phos salts in PN solutions

• Use FreAmine (B Braun) Amino Acids
  • Contains 13 mEq (10 mmol) phosphorus per 100g AA

• If no IV phosphate salts
  • NeutraPhos or NeutraPhos K 1-2 packets BID to TID
    • (1 packet = 8 mmol phos, 6.9 mEq Na, 7 mEq K)
    • Watch for exacerbations in enteral output
  • Consider reduction in IV dextrose calories
  • If serum phosphorus < 2 or symptomatic → ER

• Ensure RDs are aware of the signs/symptoms
Potassium

- Potassium Acetate
  - Use Potassium Chloride salt in PN
    - Switch all Potassium Acetate to Potassium Chloride
    - Use Sodium Acetate for acid base balance

- Potassium Chloride
  - Switch to Potassium Acetate salt in PN
  - Use sodium chloride for acid base balance
Sodium

- Sodium Acetate
  - Omit sodium acetate, do not replace with NaCl
  - Start Sodium Bicarbonate PO 650 mg BID to TID
    - Crush and take in applesauce for patients with malabsorption
  - Switch all Potassium to potassium acetate
  - Allow for hyponatremia (Na no lower than 130)
  - Allow for mild acidosis (CO2 no lower than 15)

- Sodium Chloride
  - Switch to Sodium acetate in PN
  - Use Potassium chloride to balance acid base
  - Pharmacy can use 3% NaCl in compounding process if necessary
Sodium Case Study

- PN formula
  - 100 grams AA
  - 335 grams dextrose
  - 3000 mL over 12 hrs

- KCl 100 mEq
- K Acetate 25 mEq
- NaCl 75 mEq
- Na Acetate 180 mEq

- Total Cl 175 mEq
- Total Acetate 205 mEq
- Total Sodium 255 mEq

- 35 year old male, Crohn’s Disease with high output ileostomy and fistula requiring PN

- Oral diet: bites for pleasure only

- Baseline Labs:
  - Na 138
  - Cl 102
  - CO2 26
### Sodium Case Study Continued

**PN Formula**
- **Baseline**
  - KCl: 100 mEq
  - K Acetate: 25 mEq
  - NaCl: 75 mEq
  - Na Acetate: 180 mEq

  - Total Cl: 175 mEq
  - Total Acetate: 205 mEq
  - Total Sodium: 255 mEq

**PN Formula Changes**
- KCl: 0 mEq
- K Acetate: 125 mEq
- NaCl: 175 mEq
- Na Acetate: 0 mEq

- Total Chloride: 175 mEq
- Total Acetate: 125 mEq
- Total Sodium: 175 mEq

Start Oral Sodium Bicarbonate 650 mg BID crushed in applesauce
Sodium Bicarbonate

- Oral dosing recommendations

<table>
<thead>
<tr>
<th>Serum C02</th>
<th>Recommendations Oral Sodium Bicarbonate</th>
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<tbody>
<tr>
<td>20-22</td>
<td>325 mg 3times daily</td>
</tr>
<tr>
<td>17-19</td>
<td>650 mg 3times daily</td>
</tr>
<tr>
<td>14-16</td>
<td>2- 650 mg tabs 3times daily</td>
</tr>
<tr>
<td>&lt; 14</td>
<td>IV supplementation required</td>
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Sodium bicarbonate tabs available in 325 mg or 650 mg
Sterile 98% ethanol

- Used to compound 70% Ethanol lock for prevention of catheter sepsis
  - Standard dose: 3mL of 70% ethanol lock daily while cycled PN not infusing (silicone catheters or implanted ports only)
- Recurrence of Catheter Sepsis when withheld due to shortages
- Options:
  - Decrease concentration of ethanol lock
    • from 70% to 50%
  - Decrease standard dose to every other day
  - Decrease volume
    • From 3 mL to 2 mL
  - Decrease volume and concentration
    • From standard dose to 2 mL of 50%
Increased Monitoring

• Electrolytes (Long term HPN patients)
  – Phosphorus
    – If omitting or reducing by 20 mEq – check labs in 1 week
  – Acetate
    • Check labs in 2 weeks to observe acid / base balance & K+

• Trace elements
  – With shortages - every 3 months
    • Screen for deficiencies with lack of IV product and/or use of enteral supplement
Monitoring and Safety

- Less desirable or familiar products used as alternatives
- Preventable adverse events by use of alternatives
- Increased RD assessment time and frequency of reassessment
- Increased monitoring to protect patient safety
  - Increased cost of more frequent laboratory studies

- Increased RPh compounding time
  - Confusion in prescribing process due to substitution
  - Frequent changes in compounding and distribution
  - Patches in work flow circumvent safety checks
Responsibilities

• Communicate / Publish impact of drug shortages
  • Case studies
  • Retrospective reviews

• Report medication errors
  • National Medication Errors Reporting Program
    • [https://www.ismp.org/orderforms/reporterrortoismp.asp](https://www.ismp.org/orderforms/reporterrortoismp.asp)
  • Calculation or preparation errors
  • Errors in the prescribing, transcribing, dispensing, administering, and monitoring of medications

• Increase monitoring and interdisciplinary discussion
Questions?
Additional Resources


