The Drug Shortage Crisis

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Objectives:

- Discuss drug shortages and the reasons (causes) for their occurrence
- Describe the impact of product shortages on the quality and safety of patient care
- List five actions clinicians should take in response to the PN product shortages

Financial Impact of Drug Shortages

- $216 million – Labor costs associated with managing drug shortages in the U.S.
- $200 million – Cost to purchase more expensive generic or therapeutic substitutes

Parenteral Nutrition (PN) Shortages Since Spring 2010

- Amino Acids*
- Ascorbic acid
- Calcium chloride
- Calcium gluconate
- Copper
- Cyanocobalamin
- IV fat emulsion
- L-cysteine
- Multivitamins
- Potassium acetate
- Potassium phosphate
- Selenium
- Sodium acetate
- Sodium chloride
- Sodium phosphate
- Trace elements
- Vitamin A
- Zinc

*Resolved

Notes:
- Each column represents the # of new shortages identified during that year.
- University of Utah Drug Information Service

U.S. Drug Shortages


Pharmaceutical Supply Chain

A Drug Supply Chain Example

FDA

Reasons for Sterile Injectable Shortages

- Product quality issues
- Discontinuations
- Delays/capacity
- Raw material
- Loss of manufacturing site
- Component problems/shortages
- Increase demand due to another shortage

Adapted from Jensen, FDA CDER. ISMP 2011

Effect of Drug Shortages on Patient Safety

- Institute for Safe Medication Practices
  Drug Shortages National Survey 2010
  - 1600 responses
  - 1000 errors and adverse patient outcomes due to shortages

- Premier Drug Shortage Survey 2010
  - 311 pharmacy experts
  - Hospitals and other healthcare sites
  - 89% experienced shortages that may have caused a medication safety issue or error in patient care

- A.S.P.E.N. PN Product Shortages Survey
  June-July 2011

Reasons for PN Product Shortages

<table>
<thead>
<tr>
<th>PN Product</th>
<th>Reason for Shortage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat Emulsion</td>
<td>Manufacturing or production line issues</td>
</tr>
<tr>
<td>Amino Acids</td>
<td>Consolidation of industry Raw material supply</td>
</tr>
<tr>
<td>Electrolytes/minerals</td>
<td>Manufacturing or production line issues Raw material supply Business decisions to withdraw from market</td>
</tr>
</tbody>
</table>

Hospitals Cut Doses Amid Drug Shortages

The Wall Street Journal, December 8, 2011
http://online.wsj.com/article/SB10001424052970204844504577098870278510832.html

Hospitals are grappling with a shortage of nutrition drugs and disinfectant products that has led doctors to cut doses and ration supplies, prompting patients at a handful of facilities to get sick.

The Wall Street Journal, December 8, 2011
http://online.wsj.com/article/SB10001424052970204844504577098870278510832.htm

Deaths of 9 Alabama Patients Tied to Intravenous Supplement


Effect on Safety of Parenteral Nutrition

- Less desirable or familiar product
- Confusion in prescribing process due to substitution
- Patches in work flow circumvent safety checks

Drug Shortages – the Patient Perspective

- ‘Imagine knowing your child needs vitamins – VITAMINS - and there is none available to give him knowing this will cause a decline in his health and well being and you have to, in essence, watch your child ‘starve’ because in this Great country there are drug shortages!!'
Effect of PN Product Shortages on Patient Safety

**Procurement**
- No warning of shortages
- Increased labor and time searching market for sources of products; various vendors
- Increased drug expenditures; exceed budget
- Purchase less desirable/unfamiliar products

**Management**
- Increased time and labor to develop and revise policies & procedures for alternative products, rationing measures, prescribing systems
- Difficult to keep all staff up-to-date on shortages, alternative products, changes in preparation, dispensing, etc.
- Strained relationships with providers, other health care staff, patients, families, etc.
- Time spent managing shortages vs. clinical care

**Prescribing**
- Increased prescribing errors
- Prescribe suboptimal therapy due to shortages or rationing
- Elect not to prescribe PN as unable to prevent/treat complications

**Effect of PN Product Shortages on Patient Safety**

**Procurement**
- Purchasing outside normal channels (gray or black market, compounding facility)
- Hoarding/stockpiling
- Stress on staff to find and purchase alternative products

**Management**
- Increased time and labor to develop and revise policies & procedures for alternative products, rationing measures, prescribing systems
- Difficult to keep all staff up-to-date on shortages, alternative products, changes in preparation, dispensing, etc.
- Strained relationships with providers, other health care staff, patients, families, etc.
- Time spent managing shortages vs. clinical care

**Prescribing**
- Unable to keep up with shortages, alternative products, rationing, restrictions, etc.
- Prescribing process constantly changing based on product availability, alternative products, rationing, etc.
- Work arounds that may circumvent safety checks
Effect of PN Product Shortages on Patient Safety

Order Review
- Difficulty keeping up-to-date on shortages, alternative products, etc.
- Work arounds may circumvent safety checks
- Increase number of prescribing errors
- Increase number of phone calls to correct or clarify orders
- Strained relationships with providers and health care colleagues

Effect of PN Product Shortages on Patient Safety

Compounding & Dispensing
- Difficult/stressful trying to keep up-to-date on shortages, alternative products, rationing, etc.
- Work arounds that circumvent safety checks
- Using unfamiliar products

Effect of PN Product Shortages on Patient Safety

Compounding & Dispensing
- Using products similar in appearance
- Increased manipulation of products
- Transfer of product from original container
- Pooling of small volumes into larger source containers

Effect of PN Product Shortages on Patient Safety

Compounding & Dispensing
- Preparation of sterile injectables from source powders
- PN orders and bag labels may not match due to frequent changes in order process, alternative products, rationing, etc.

Effect of PN Product Shortages on Patient Safety

Administration
- Difficult/stressful trying to keep up-to-date on shortages, alternative products, rationing, etc.
- PN orders and bag labels may not match due to frequent changes in order process, alternative products, rationing, etc.
- Necessary to administer additional IV supplements (e.g. Ca chloride)
- Increased infection risk when accessing intravascular access multiple times to administer supplements
### Effect of PN Product Shortages on Patient Safety

#### Monitoring
- Increased costs for additional labs to monitor for deficiencies or complications
- Increased time to monitor and review lab results and revise patient care plans

#### Effect of PN Product Shortages on Patient Safety

#### Patient Outcomes
- Deficiencies due to vitamin shortages
  - Thiamin-lactic acidosis
  - Vitamin A-night blindness
  - Multiple deficiencies when stopped oral vitamins
- Contaminated PN resulting in deaths
- Amino acids shortage
- Hypophosphatemia due to giving less/none

#### Patient Outcomes
- Unable to provide neonates with adequate calcium and phosphorus for bone accretion due to lack of L-cysteine used to enhance solubility
- Hyperkalemia from administering oral Na/K phosphate products to patients who needed P but not K
- Hyperglycemia when increasing dextrose intake to meet energy needs when IV fat emulsion not available

#### Patient Outcomes
- Hyperchloremic metabolic acidosis due to lack of acetate salts
- Hyponatremia due to lack of sodium products
- Increased incidence of refeeding syndrome
- Electrolyte abnormalities after changing to amino acid product containing electrolytes or different electrolyte profile during amino acids shortage

#### Patient Outcomes
- Fluid overload due to preparing PN’s with less concentrated amino acids and IV fat emulsion
- Diarrhea when administering oral electrolyte supplements
- Increased catheter-related blood stream infections when ethanol locks unavailable
- Increased infection risk when accessing intravascular access to administer supplements

#### Patient Outcomes
- Increased hospitalizations for electrolyte abnormalities or catheter-related infections
- Unable to transfer patients from acute care hospitals to SNF’s or LTACH’s due to increased cost of PN’s
- Patients transferred to another hospital for PN therapy
Managing Parenteral Nutrition Product Shortages

- Recommendations for shortages
  - Multivitamins – adult and pediatric
  - IV fat emulsions
  - Amino acids
  - Electrolytes/minerals
  - Trace elements – adult and pediatric
  - L-cysteine
- A.S.P.E.N. web site www.nutritioncare.org
- Search specific product shortage
- Professional Resources>A.S.P.E.N. Documents Library

Shortages Information Resources

- FDA Center for Drug Evaluation and Research (CDER) Drug Shortage Program (DSP)
  - Potential or actual shortages
  - Medically necessary products
- ASHP Drug Shortages web site
  - All medication shortages
- A.S.P.E.N. Documents Library
  - Considerations for Managing PN Product Shortages
- Manufacturer’s web site

Managing PN Product Shortages

Drug Shortage Legislation

- Drug Shortage Prevention Act
- Intra-agency communication at FDA
- Communication between FDA, distributors, providers and patients
- Definitions
  - Critical drug
  - Critical drug shortage
  - National Critical Drug List
  - National Critical Drug Shortage List

A.S.P.E.N. Collaboration

- Food and Drug Administration
- American Society of Health-System Pharmacists (ASHP) www.ashp.org/shortage
- A.S.P.E.N. Staff And Volunteers
- Institute for Safe Medication Practices (ISMP)
- Manufacturers
- A.S.P.E.N. members and non-members

Conclusion

- The drug shortage crisis is a threat to the safest pharmaceutical supply chain in the world which has impacted the access to and quality of PN therapy in the U.S. health system
- Collaboration with health care professionals, professional societies, regulatory and accrediting bodies as well as manufacturers is necessary to avoid major problems in the care of patients receiving PN